ANAL SPHINCTERS, SUPPORT STRUCTURES AND ATROPHY IN MAJOR OBSTETRIC INJURY

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DECLARATION OF AUTHORSHIP AND ORIGINALITY

I, Dipal Patel confirm that the work presented in this thesis is my own. Where information has been derived from other sources, I confirm that this has been indicated in the thesis.

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ABSTRACT

Mechanical anal sphincter trauma and traction pudendal neuropathy secondary to vaginal childbirth represent the most frequent aetiological factors in the development of faecal incontinence in women. More recently it has been speculated that vaginal childbirth may damage pelvic support structures, thereby contributing to faecal incontinence. Anal sphincter and pelvic floor atrophy resulting from degenerative pudendal neuropathy is thought to also play an important aetiopathogenic role. Measurement of puborectalis function is therefore essential in providing a baseline assessment and observing response to treatment of puborectalis muscle strength in pelvic floor dysfunction disorders.

Until recently there has been difficulty in understanding the role of puborectalis function due to the absence of a standardised measurement technique. So far, Magnetic Resonance Imaging (MRI) has been proposed for accurate structural assessment however, no consensus has yet been reached on the 'gold standard' for the physiological measurement of puborectalis strength.

This thesis primarily looked at finding novel structural and physiological measures of puborectalis in a cohort of asymptomatic nulliparous controls, women with clinically reported obstetric anal sphincter injuries and women with idiopathic faecal incontinence.

The first technique I used was vaginal manometry to quantify the constrictor function of puborectalis. I was unable to show the previously reported specific high pressure vaginal zone in either study groups and I found poor agreement between vaginal and anorectal manometry in the measurement of pelvic floor squeeze.

The second technique I used was the 2 point Dixon fat water decomposition MRI technique to quantify fatty atrophy of the anal sphincter complex and puborectalis. I was able to demonstrate a relationship between external anal sphincter percentage fat content with both patient symptom load and subjective atrophy score demonstrating it as a promising objective measure of fatty atrophy.

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ETHICAL APPROVAL

All the studies contained within this thesis involving both healthy volunteers and patients were approved by the National Hospital for Neurology and Neurosurgery and Institute of Neurology Research Ethics Committee (project reference number 10/H0716/10). All subjects were given a comprehensive information leaflet explaining the study in which they were participating in. Informed written consent was obtained from all study participants.

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CHAPTER ONE

OBSTETRIC ANAL SPHINCTER INJURY

1.1 Introduction

Anal incontinence is defined as the involuntary loss of faeces or flatus. It is a socially isolating, physically and psychologically disabling pathological condition that often has profound consequences on all aspects of quality of life. Faecal incontinence is rarely attributable to a single factor but usually results from the interplay of multiple pathogenic mechanisms. The most common causes include obstetric or surgical traumatic sphincter defects, neurological dysfunction of the pelvic floor musculature and rectal prolapse (Law et al. 1991; Jorge and Wexner 1993; Rociu et al. 1999). Women comprise the majority of affected individuals with the burden of incontinence being most often related to obstetric factors. My thesis is directed towards gaining a better understanding of how best to assess the problem of post obstetric faecal incontinence.

This chapter outlines the mechanisms and risk factors involved in disruption of continence focussing primarily on obstetric related anal sphincter and pelvic floor injury. This will then be followed with a description of the evolving areas of our understanding regarding investigation in this particular patient group.

1.2 Mechanisms involved in disruption of continence

Vaginal delivery represents the single most important aetiological factor in the development of faecal incontinence in women (Donnelly et al. 1998). There are three ways in which childbirth can lead to injury of the anal sphincter mechanism:

1) Direct anal sphincter muscle trauma most commonly occurring during first vaginal delivery (Snooks et al. 1990)

2) Indirect injury secondary to traction pudendal neuropathy leading to progressive disruption of the pelvic floor musculature with successive deliveries (Snooks et al. 1990).

3) Combined neurological and mechanical sphincter trauma.

1.3 Classification of perineal tears

Up until recently no standardised criteria was set in place for the classification of obstetric anal sphincter injuries, resulting in the under-estimation of complete or partial EAS and IAS tears as second degree tears. In 1999, Sultan proposed the following grading system which has since been adopted by the International Consultation on

Incontinence, The Royal College of Obstetricians and Gynaecologists 2001 and the World Health Organisation (Norton et al. 2002).

First degree: Injury to the vaginal epithelium or perineal skin only.

Second degree: Injury to the superficial perineal muscles only.

Third degree: Injury to the anal sphincter complex, which is further subdivided into

3a: Less than 50% of EAS thickness torn

3b: More than 50% of EAS thickness torn

3c: IAS also torn

Fourth degree: Injury to both external and internal anal sphincter muscles extending into the anal epithelium or rectal mucosa.

Obstetric anal sphincter injury encompasses both third and fourth degree perineal tears.

1.4 Obstetric anal sphincter disruption

The overall incidence of clinically recognised obstetric anal sphincter injury varies widely between countries and cohorts studied and has been reported to be between 0.6 to 10.8% (Sultan et al. 1994; Robinson et al. 1999). Difficulty in estimating the true incidence of third and fourth degree sphincter tears occurs due to variation in the tools used to detect injury (clinical examination vs anal endosonography) along with different hospital policies regarding the use of instrumentation and the type and indications for episiotomy. Therefore caution must be taken when comparing incidence rates of obstetric tears between different institutions. The introduction of endoanal ultrasound has led to a higher incidence of clinically undetected injury at the time of delivery being identified in upto 36% of women after vaginal delivery (Donnelly et al. 1998; Williams et al. 2001). Despite primary sphincter repair the outcome is suboptimal, with studies reporting between 30 to 50% of women experiencing ongoing symptoms of impaired faecal continence, faecal urgency, perineal pain and dyspareunia (Sultan et al. 1994; Zetterstrom et al. 1999; Sangalli et al. 2000; de Leeuw et al. 2001; Fitzpatrick et al. 2000; Williams 1999; Davis et al. 2003; Pinta et al. 2004; Mackenzie et al. 2004).

Although we are aware of the risk factors associated with anal sphincter trauma the majority are not modifiable and only become apparent late in labour and therefore cannot be predicted or controlled for to prevent the occurrence of a third or fourth degree tear. In addition, many of the labour and delivery decisions are often dependent on complex inter-related risk factors. In cases of foetal distress the use of episiotomy

and operative vaginal delivery may be inevitable and although they are well known major risk factors for anal sphincter tears they remain amongst the few obstetric factors which can be controlled by obstetricians and midwives (Kudish et al. 2006).

At present it has not been possible to develop an antenatal risk scoring system which can accurately predict if a woman is susceptible to sustaining an obstetric sphincter injury (Williams et al. 2005). Such an instrument would improve risk assessment for vaginal delivery both for the obstetrician and patient (Gudmundsson et al. 2005).

1.5 Predictive antenatal risk factors

A number of studies have identified several risk factors contributing to obstetric anal sphincter trauma. These include antenatal factors such as birth weight of greater than 4kg, nulliparity, persistent occipitoposterior position and induction of labour; and intrapartum factors such as epidural analgesia, instrumental delivery (forceps and ventouse), episiotomy and prolonged second stage of labour (Adams et al. 2001). However, much of the evidence between these studies remains contradictory.

In addition to the risk factors mentioned above there are other predisposing factors such as race, obesity and collagen weakness which are less widely understood.

1.5.1 Race

Regarding maternal race and the rate of third and fourth degree tears, afro-Caribbean women have been reported to have a lower incidence of perineal trauma in comparison to Caucasian women (10% vs 20%) (Howard et al. 2000). In a retrospective study carried out over a 5 year time period of over 2 million vaginal deliveries Handa et al. 2001 found Indian (OR 2.5 95% CI 2.23, 2,79) and Filipina (OR 1.63 95% CI 1.50, 1.77) women to be at the highest risk of sustaining obstetric anal lacerations. Possible biological explanations for these differences have been suggested and include short stature, variation in collagen content of connective tissue and shortened perineal body (Van-Dongen 1981; Green and Soohoo 1989; Combs et al. 1990).

1.5.2 Collagen composition

In a prospective cohort study of 549 nulliparas, Chaliha et al. 1999 failed to show a relationship between physical markers of collagen weakness e.g. the presence of abdominal striae, hernia, varicose veins and joint hypermobility and the pathogenesis of postpartum faecal and urinary incontinence. The authors concluded, "Although collagen weakness was previously implicated in pathogenesis of incontinence, physical markers in this study could not predict postpartum urinary and fecal incontinence. Either those markers were not representative of collagen weakness, or a larger study with longer follow up is necessary" (Chaliha et al. 1999). However, Lind and Wallenburg 2002 studied the effect of connective tissue disease on pregnancy and reported an increased rate of third degree tears (10% vs 0%) along with perineal wound dehiscence and wound infection (10% vs 0%) in women with Ehlers-Danlos syndrome compared with healthy women.

1.5.3 Obesity

Maternal obesity is associated with an increased risk of adverse outcomes during the antepartum, intrapartum and postpartum periods in comparison to women with a normal body mass index (Kabiru and Rayner 2004). Regarding complications relating to delivery, obese pregnant women are at increased risk of both operative delivery and perineal lacerations which are closely related to foetal macrosomia (Voldner et al. 2009).

1.5.4 Foetal birthweight

A number of studies have reported an association between increased foetal birthweight and anal sphincter tears. De Leeuw et al. 2001 in one of the largest population based observational studies of 284,783 births found a significant positive correlation between the incidence of third degree sphincter tears and birthweight. Multiple logistic regression analysis used to isolate inevitably interlinked obstetric events showed an odds ratio of 1.47 with each increase of birthweight by 500g (De Leeuw et al. 2001). This association presumably occurs as a result of larger mechanical stresses being placed upon the perineum during the delivery of a larger baby. Similarly, Samuelsson et al. 2000 in a prospective observational study of 2883 births found high infant birthweight (>4000g) to be associated with anal sphincter tears on univariate analysis (OR 3.27), but on stepwise logistic regression analysis high birthweight was found to be

not as influential a risk factor in parous women, which is in agreement with a previous study (Poen et al. 1997). One possible explanation for this observation is the difference in strength and laxity of the connective tissue between the nulliparas and multiparas. These findings have been shown in several other studies (Zetterstrom et al. 1999; Poen et al. 1998; Handa et al. 2001; Richter et al. 2002; Parnell et al. 2001; Jander and Lyrenas 2001; Andrews et al. 2006; Gupta et al. 2003; Jander and Lyrenas 2001; Bodner-Adler et al. 2001; Angioli et al. 2000; Christianson et al. 2003).

1.5.5 Foetal presentation

Foetal presentation is an important factor in the occurrence of obstetric sphincter tears. A persistent occipitoposterior position of the foetal head has been reported to have a significantly increased risk of anal sphincter damage along with a higher incidence of instrumental assisted delivery, episiotomy and caesarean section (Poen et al. 1997; Bek and Laurberg 1992; Sultan et al. 1994; Wu et al. 2005; Fitzpatrick et al. 2001; Dudding et al. 2008).

The factors discussed above carry unalterable risks in the development of obstetric anal sphincter tears. The following section will now focus on the potentially modifiable risk factors for anal sphincter injury.

1.6 Intrapartum risk factors

1.6.1 Epidural analgesia and duration of second stage of labour

The use of epidural analgesia during labour has increased in popularity since the 1980s but little attention has been paid to its possible effects on the perineum and pelvic floor (Fitzpatrick and O'Herlihy 2000). In theory, epidural analgesia abolishes the bearing down reflex and permits passive prolongation of the second stage of labour facilitating controlled delivery of the foetal head thus minimising the need for episiotomy and operative delivery and consequently resulting in fewer anal sphincter tears. Conversely, pain which normally acts as an alarm for perineal overstretching is inhibited by epidural analgesia thus increasing the risk of sphincter trauma (Gerdin et al. 2007).

The relationship between epidural analgesia and perineal trauma is difficult to delineate due to the effect of multiple confounding factors and as a result has led to conflicting data between published studies. Donnelly et al. 1998 conducted a prospective study on

168 primiparous women and found a significant association between use of epidural analgesia and prolonged second stage of labour, increased risk of sphincter injury and incontinence symptoms. Multiple logistic regression analysis showed that use of epidural analgesia resulted in a 7.7 fold (P=0.004; 95% CI 4.0-14.7) increase in the length of the second stage of labour and was associated with increased risk of symptoms (OR 2.0; P=0.02; 95% CI 1.1-3.7) and anal sphincter injury (OR 2.1; P=0.02; 95% CI 1.1-4.0). The authors concluded that a second stage of labour prolonged by the use of epidural analgesia posed the greatest risk of injury to the anal sphincter complex and pudendal nerves resulting in subsequent incontinence symptoms in primiparous vaginal delivery.

Other possible causes of anal sphincter injuries secondary to epidural analgesia may relate to increased use of episiotomies and more instrument assisted deliveries being performed (Robinson et al. 1999; Erikkson et al. 2006; Liu and Sia 2004). Several other studies have reported an increased risk of sphincter injury with epidural use (ref Poen et al. 1997; Gerdin et al. 2007; Robinson et al. 1999). In contrast some studies have demonstrated a protective effect of epidural analgesia with no association of anal sphincter injury (Eskander and Shet 2009; Samuellson et al. 2000; Williams 2003; Dahl and Preben 2006; Baumann et al. 2007). A possible explanation for these differences in outcomes could be accounted for by the use of nulliparous versus mixed parity women as study groups. Studies reporting an increased risk of sphincter tear with epidural use included nulliparous women only where pain which normally functions as an alarm for perineal overstretching is lost. Where as in multiparous women, who are hypothesised to have stronger yet more lax perineal musculature, epidural use produces an additional effect of relaxation of the perineal muscles resulting in a decreased risk of sphincter injury.

With regards to length of second stage as a single risk factor for anal sphincter tears, earlier studies have failed to show a relationship between these two events (Bek and Laurberg 1992; Poen et al. 1997; Wilcox et al. 1989; Green and Soohoo 1989). Bek and Laurberg 1992 were one of the first to show an association between prolonged second stage of labour and incidence of sphincter injury (adjusted OR 1.6) which has since been confirmed by subsequent studies (Cheng et al. 2004; Fraser et al. 2000). It is thought that a prolonged duration of second stage subjects the perineum to a longer

period of stretching resulting in increased ischaemic rupture of the perineal and anal sphincter muscles. A large retrospective cohort study of 15,759 nulliparous women found that a prolonged second stage did not affect neonatal morbidity but was associated with increased rates of anal sphincter tears and operative vaginal deliveries (Cheng et al. 2004). Thirty four percent of women who had a second stage of greater than 4 hours sustained a third or fourth degree sphincter tear, which, after being controlled for confounders still remained a statistically significant risk factor (OR 1.33). The question still remains as to what point the second stage truly becomes too long (Cheng et al. 2004).

Although it is evident that the risk of anal sphincter injury is elevated with a prolonged duration of second stage of labour there is also an increase in operative vaginal deliveries which in itself carries a high risk of sphincter injuries (Cheng et al. 2004; De Leeuw et al. 2001). Further long term prospective studies are required to address this issue.

1.6.2 Episiotomy

As yet absolute indications for the use of episiotomy remain to be established (Dudding et al. 2008).

Episiotomy is the most commonly performed intervention during vaginal delivery. Suggested theoretical benefits include shortening the second stage of labour, reducing the risk of major perineal damage and subsequent pelvic floor dysfunction, creation of a clean cut instead of a spontaneous tear improving tissue apposition during primary repair along with promoting wound healing and protection of the neonate from delivery trauma (Thacker and Banta 1983). The rate of episiotomy varies considerably worldwide reflecting differences in obstetric practice (Dudding et al. 2008). The national rate of performed episiotomies in the UK and USA has decreased over the years with an estimated rate of 16% and 35% respectively (Revicky et al. 2010; Hartmann et al. 2005).

There are 3 types of episiotomy currently in use: midline (vertical incision from the posterior fourchette towards the rectum) which is more commonly employed in USA, mediolateral (incision 40 degrees from the midline towards the ipsilateral ischial

tuberosity) the method of choice in Europe and anterior (deinfibulation) performed in women with previous female circumcision (Cleary-Goldman and Robinson 2003; Eogan et al. 2006).

A number of studies have reported a strong association between midline episiotomy and incidence of sphincter trauma but interestingly no study has ever shown it to be protective (Gerdin et al. 2007; Helwig et al. 1993; Combs et al. 1990; Labrecque et al. 1997; Woolley 1995; Klein et al. 1994; Zetterstrom et al. 1999; Bodner-Adler et al. 2001; Jander and Lyrenas 2001). In a randomised controlled trial Coats et al. 1980 reported midline episiotomy to be associated with a higher rate of third and fourth degree tears in comparison with mediolateral episiotomy (11.6% vs 2% n=407) (table 1.1). Several studies have since confirmed this finding (Signorello et al. 2000; Zetterstrom et al. 1999; Shiono et al. 1990).

Table 1.1 Incidence of 3rd and 4th degree tears in association with midline or mediolateral episiotomies (Cleary-Goldman and Robinson 2003).

Author	Year	Type of Study	Number of patients	3rd/4th degree tears with midline episiotomy	3rd/4th degree tears with mediolateral episiotomy
Coats et al.	1980	Randomised control trial	407	19/163 (11.6%)	5/244 (2%)
Shioni et al.	1990	Prospective multicentre	24,114	781/8045 (9.7%)	153/8655 (1.8%)
Anthony et al.	1994	Observational	43,305	13/556 (2.3%)	68/12,736 (0.5%)
Angioli et al.	2000	Retrospective	50,210	294/4430 (6.6%)	614/13,361 (4.6%)
De Leeuw et al.	2001	Observational 3rd degree tear only	284,783	109/3614 (3%)	1234/97250 (1.3%)

The data concerning the role of mediolateral episiotomy in the prevention of sphincter trauma remains more controversial. Possible reasons for conflicting results may be due to variation in the angle of mediolateral episiotomy performed and the comparison of data generated from midline episiotomies with mediolateral episiotomies. Some studies have suggested that mediolateral episiotomy is associated with an increased risk of sphincter injury (Walsh et al. 1996; Bek and Laurberg 1992; Argentine Episiotomy Trial Collaborative Group 2003) (table 1.2) whilst others have shown a strong protective effect (Aukee et al. 2006; Poen et al. 1997; de Leeuw et al. 2001; Revicky et

al. 2010; Dahl and Preben 2006; Dandulo et al. 2005; Handa et al. 2001) (table 1.3) or no association between mediolateral episiotomy and sphincter trauma (Henriksen et al. 1992; Buekens et al. 1985). However conclusions drawn from some of these studies must be made with caution due to small numbers or lack of analysis of confounding variables by multiple regression techniques.

De Leeuw et al. 2007 in a large retrospective observational study using the Dutch National Obstetric Database reported a strongly protective effect of mediolateral episiotomy against third degree sphincter tears. More recently, Revicky et al. 2010 performed the largest retrospective UK study (n=10,314) regarding risk factors for obstetric sphincter tears analysed by multiple logistic regression. They showed mediolateral episiotomy to be associated with a lower incidence of sphincter injury. In both studies the incidence of third and fourth degree tears may have been under reported as endoanal ultrasonography was not performed to confirm the true incidence of obstetric sphincter tears in these patients.

Table 1.2 Studies reporting association between mediolateral episiotomy and anal sphincter tears.
*adjusted odds ratio (OR)

Author	Year	Type of study	Number of patients	Number or % of patients with anal sphincter tears with M/L episiotomy	OR
Bek and Laurberg	1992	Case control	41,200 152 sphincter tear 304 controls	85%	2.8 *
Walsh et al.	1996	Prospective 3rd degree tear only	16,583 93 3rd degree tear	74%	-
Williams et al.	2003	Retrospective 3rd degree tear only	10,382 75 sphincter tear 10307 controls	33%	2.58

Table 1.3 Studies reporting protective effect of mediolateral episiotomy with anal sphincter tears.
* third degree tears in primips
** Vaginal deliveries with no ML episiotomy had a 1.4 times greater risk of a sphincter tear compared to subjects who did have a ML episiotomy.

Author	Year	Type of study	Number of patients	Number or % of patients with anal sphincter tears with M/L episiotomy	OR
Aukee et al.	2006	Retrospective 3rd degree only	9231 53 sphincter tear 9178 controls	48%	0.37
Poen et al.	1997	Retrospective	6683 120 sphincter tear 702 controls	50%*	0.46*
De Leeuw et al.	2001	Observational 3rd degree only	284,783 5528 sphincter tear 279,255 controls	-	0.34
Handa et al.	2001	Retrospective	2,101,843 123,009 sphincter tears 1,978,834 controls	-	0.81 3rd degree tears (1.12 4th degree tears)
Revicky et al.	2010	Retrospective	10,314 332 sphincter tears 9982 controls	-	1.4**
Dandolu et al.	2004	Retrospective	258,507 18,888 sphincter tears 239,619 controls	7%	0.9

One must also note that the majority of the studies mentioned above analysed the primiparous and multiparous women together which potentially has an effect in the outcomes and should be considered as an important limitation. A recent study (Raisanen et al. 2009) aimed to determine the effect of mediolateral episiotomy on anal sphincter trauma amongst individual primiparous and multiparous groups. Interestingly following multivariate analysis, episiotomy in the primiparous group was associated with a decreased risk of obstetric tear (OR 0.83) where as in the multiparous group, episiotomy was associated with an increased risk of sphincter tear (OR 2.01). The authors put this observation down to more complicated deliveries secondary to multiple risk factors in the multiparous women.

A Cochrane review of 5 randomised controlled trials (Argentine Episiotomy Trial Collaborative Group 2003; Harrison et al. 1984; House et al. 1986; Sleep et al. 1984. Klein et al. 1994; Carroli et al. 1999) assessed the outcome following restrictive and routine mediolateral episiotomy at vaginal delivery. They reported less perineal trauma in the restrictive episiotomy group compared with the routine group (OR 0.88).

Concerns have recently been raised that not all episiotomies are the same in terms of length and angulation resulting in mediolateral episiotomies not being truly mediolateral but more midline (Andrews et al. 2006). Tincello et al. 2003 used a pictorial questionnaire to highlight that both doctors (2%) and midwives (23%) performed mediolateral episiotomies more towards to the midline than mediolateral. In addition the mediolateral episiotomies drawn by the doctors were significantly longer and more angled away from the midline in comparison to the midwives'. Eogan et al. 2006 in a case controlled study demonstrated a 50% relative risk reduction of sustaining a third degree tear for every 6 degrees away from the midline the episiotomy was made. A similar study performed by Andrews et al. 2006 showed that mediolateral episiotomies that are angled closer towards the midline are at significantly increased risk of sphincter injuries (26 degrees with injury vs 37 degrees with no injury p=0.01). No midwives and only 13 (22%) obstetricians performed a true mediolateral episiotomy which indicates the need for re-examination of the role of the correct episiotomy technique (Andrews et al. 2006). These findings are clinically relevant and also highlight the necessity for more structured and standardised training in performing a mediolateral episiotomy (Andrews et al. 2006) which can potentially lead to a reduction in the rates of obstetric sphincter injuries and their sequelae.

Episiotomies tend to be used in combination with instrumental deliveries. It is well established that midline episiotomies in operative vaginal deliveries is strongly associated with third and fourth degree sphincter tears (Helwig et al. 1993; Robinson et al. 1999; Kudish et al. 2006; Wu et al. 2005; Benavides et al. 2005). Kudish et al. 2006 found that the joint use of forceps and midline episiotomy resulted in a 20 fold and 77 fold increase in the rate of sphincter tears in nulliparas and multiparas respectively in comparison to vaginal delivery alone. The authors hypothesised that the two surgical modalities work synergistically with eachother resulting in an amplified effect of stress and stretch on the anal sphincter mechanism. The effect of mediolateral episiotomy and operative vaginal delivery still remains a subject of debate. Youseff et al. 2005 demonstrated an increased risk of sphincter tears with mediolateral episiotomy used in operative vaginal deliveries however this risk was abolished after separate analysis of vacuum extractions and forceps deliveries. Several lines of evidence have reported a protective effect of mediolateral episiotomy on vacuum and forceps deliveries both separately and in combination (Combs et al. 1990; Bodner-Adler et al. 2003; Aukee et

al. 2006; De Leeuw et al. 2007). Limitations of the majority of these studies are based on their retrospective nature, lack of randomisation and variation in training levels of obstetricians performing the deliveries in combination with differing techniques used between countries.

1.6.3 Instrumental delivery

Operative vaginal delivery is performed in 10-13% of women in the UK (Beukens et al. 1985; Anthony et al. 1994). The indications for operative intervention are presumed foetal compromise, to shorten the second stage of labour in certain medical conditions such as myasthenia gravis and hypertensive crisis and failure to progress which is defined as lack of continuing progress without regional anaesthesia for 2 hours in nulliparas and 1 hour in multiparas (RCOG green top guideline number 29).

It is well documented that all types of instrumental assisted vaginal deliveries significantly increase the risk of anal sphincter tears particularly in combination with episiotomy (de Leeuw et al. 2001; Christianson et al. 2003; Dandolu et al. 2005; Thacker and Banta 1983). The association between operative delivery and obstetric sphincter tear has been demonstrated by endoanal ultrasonography (Belmonte-Montes et al. 2001).

Interpretation and comparison of studies investigating the impact of instrumental assisted deliveries on the incidence of anal sphincter injury is difficult due to the different types of forceps and vacuum or ventouse extractors currently in use. Despite this, a number of retrospective studies have shown unequivocal agreement that forceps assisted vaginal delivery is an independent risk factor for anal sphincter tears (Baumann et al. 2007; de Leeuw et al. 2001; Poen et al. 1997; Combs et al. 1990; Riskin-Mashiah et al. 2002; Angioli et al. 2000; Christianson et al. 2003; Richter et al. 2002). In theory forceps cause more damage than ventouse extractors as the blade occupies a larger area of the pelvic outlet exerting greater pressure on the perineum during traction (Sultan et al. 1993).Up until now two of three prospective studies evaluating the risk of anal sphincter injury with forceps assisted delivery have failed to show any association (Zetterstrom et al. 1999; Shiono et al. 1990). The third prospective study carried out by Donnelly et al. 1998 found an 8.1 fold risk of anal sphincter injury with instrumental assisted deliveries. However, the study is weakened by small numbers undergoing

instrumental delivery (22 of 168 women) and lack of distinction made between the type of instrumental delivery performed. One possible explanation for the high association between sphincter tears and forceps deliveries in previous work may be due to under diagnosis of third and fourth degree sphincter tears in women having non instrumental deliveries (Andrews et al. 2006). Secondly, it may reflect how management of deliveries has changed with time with vacuum extraction being the instrument of choice and forceps being reserved for more complex cases (Andrews et al. 2006).

In comparison to forceps assisted delivery a number of studies have shown vacuum assisted delivery to be associated with a significantly lower risk of anal sphincter trauma (Johansen and Menon 2000; de Leeuw 2001; Combs et al. 1990; Crawford et al. 1993; Sultan et al. 1994; Poen et al. 1997; Williams et al. 2003; Andrews et al. 2006; Baumann et al. 2007; Dandolu et al. 2005). A disadvantage of the vacuum approach is that there is a higher likelihood of failure of successful delivery with progression to the use of forceps which carry additional further risks to both mother and baby. In a systematic review of seven randomised controlled trials comparing the incidence of sphincter trauma with forceps and vacuum delivery, Eason et al. 2000 reported a 6% absolute risk reduction in perineal trauma with vacuum delivery when compared to forceps delivery (Dandolu et al. 2005). The majority of these studies however did not confirm the presence of sphincter tears with endoanal ultrasonography resulting in over or under estimation of the true incidence of tears in association with instrumental delivery. Sultan et al. 1993 found the number of sonographically confirmed anal sphincter defects to be significantly higher following forceps delivery (P=0.0002, 81%, 21 of 26 women) in comparison to ventouse delivery (24%, 4 of 17 women) and normal vaginal delivery (36%, 17 of 47 women). In contrast, Fitzpatrick et al. 2003 performed a large randomised control trial (n=130) and found no difference in the number of sphincter defects sustained with forceps or ventouse delivery. However, 3 months post delivery symptoms of altered faecal continence were significantly more common in the forceps assisted delivery group than the vacuum assisted delivery group (59% vs 33% p=0.006).

Combined use of forceps and ventouse extraction has been demonstrated to increase the risk of obstetric sphincter tears in comparison to the use of one instrument alone and therefore should be avoided (Donnelly et al. 1998; de Leeuw et al. 2001).

Current guidelines from the Royal College of Obstetricians and Gynaecologists regarding operative vaginal delivery state "the operator should choose the instrument most appropriate to the clinical circumstances and their level of skill" (RCOG green top guidelines number 29).

Table 1.4 Risk factors associated with obstetric anal sphincter lacerations.
*Univariate logistic regression analysis
** Multivariate logistic regression analysis
*** Reference=yes hence not having an episiotomy is associated with a 1.46 times likely risk in sustaining an anal sphincter tear
**** mediolateral episiotomy

Risk Factor	Samuelsson* et al. 2000 n=2883 Tear=95 Multips & primips	De Leeuw* et al. 2001 n=284,783 Tear=5528 Multips & primips	Gerdin** et al. 2007 n=1130 Tear=565 Multips & primips	Raisanen** et al. 2009 n=217,778 Tear=2315 Primips	Revicky** et al. 2010 n=10,314 Tear=332 Multips & primips
	OR (95% confidence interval)				
Primiparous	6.51 (2.36-17.95)	2.39 (2.24-2.56)	4.87 (3.54-6.71)	-	3.19 (2.50-4.09)
Episiotomy	2.34 (1.42-3.85) ****	0.21 (0.19-0.23)****	2.12 (1.58-2.86)	0.83 (0.75-0.92)	1.46*** (1.05-2.05)
Occipito-posterior foetal presentation	1.88 (0.80-4.40)	1.73 (1.52-1.98)	-	3.17 (1.64-6.15)	-
Foetal birthweight > 4000g	3.27 (1.32-8.10)	-	2.96 (2.13-4.10)	4.66 (3.86-5.63)	12.9 (2.78-59.88)
Forceps	-	3.53 (3.11-4.02)	-	10.2 (3.60-28.90)	3.98 (2.64-5.99)
Ventouse	4.06 (2.34-7.05)	1.68 (1.52-1.86)	-	3.88 (3.25-4.63)	2.28 (1.65-3.15)
Instrumental delivery	-	-	3.28 (2.10-5.11)	-	-
Second stage > 60 minutes	5.19 (2.66-10.13)	-	-	2.06 (1.65-2.58)	-
Epidural	2.23 (1.48-3.38)	-	2.15 (1.37-3.37)	0.79 (0.73-0.87)	0.8 (0.61-1.07)

1.7 Faecal incontinence and obstetric anal sphincter injury

Despite primary repair of third and fourth degree anal sphincter tears the functional outcome is often disappointing with studies reporting a high prevalence of faecal

incontinence (range 40-50%) mainly due to persisting sphincter defects (Sultan et al. 1994; de Leeuw et al. 2002; Poen et al. 1998; Poen et al. 1997; Crawford et al. 1993; Tetzschner et al. 1996). The majority of these symptomatic women have minor reported symptoms with 5-26% of women being incontinent to flatus and 1-6% of women with frank faecal incontinence within the first year after vaginal delivery (Chaliha et al. 1999; Zetterstrom et al. 1999; Grouz et al. 1999; Sultan et al. 1993; Donnelly et al. 1998; Hall et al. 2003). Limitations of studies carried out thus far include small study sizes, short follow up periods, lack of comparative control groups and failure to distinguish outcome of third and fourth degree tears as two separate groups. Variability between results may also be accounted for by lack of consistency in validated symptom score questionnaires used and the variation in definition of severity of symptoms.

The risk factors most consistently reported to be independently associated with the development of faecal incontinence include instrumental delivery in particular forceps delivery (Pretlove et al. 2008; Hatem et al. 2007) and the degree of anal sphincter tear (de Leeuw et al. 2001; Poen et al. 1998; Haadem et al. 1998; Pollack et al. 2004; Eason et al. 2002; Zetterstrom et al. 1999; Chaliha et al. 1999; Richter et al. 2006; Starck et al. 2006; Nazir et al. 2002). Recent studies also demonstrate a significantly higher prevalence of anal incontinence symptoms in women with a history of fourth degree anal sphincter tears compared with third degree tears (25% vs 11.5% Sangalli et al. 2000; 30.8% vs 3.6% Fenner et al. 2003; 59% vs 28% Nichols et al. 2005; Norderval et al. 2005; de Leeuw et al. 2001). The prevalence of symptoms not only depends on the degree of anal sphincter injury but also the primary method of repair although it remains to be established which surgical technique (overlap or end to end approximation) is superior. Transient faecal incontinence immediately following vaginal deliveries complicated by anal sphincter tears has also been reported to be a predictor of deterioration of continence following subsequent deliveries (Bek and Laurberg 1992).

Other studies have reported faecal and flatal incontinence in women with no clinically diagnosed sphincter tear which may indicate the presence of an occult sphincter injury or pudendal neuropathy (Sultan et al. 1993; Zetterstrom et al. 1999; Fenner et al. 2003). Sultan et al. 1993 were the first to hypothesise that women with an occult sphincter injury confirmed by postpartum endoanal ultrasonography were at a higher risk of developing faecal incontinence later in life. Haadem et al. 1988 and Zetterstromet al.

1999 have presented conflicting outcomes on the incidence and severity of faecal incontinence symptoms at 5 and 9 month follow up between women with sphincter tears and women with intact sphincters. Zetterstrom et al. 1999 found 54% of women with a primarily repaired sphincter tear were incontinent at 5 months with 41% remaining symptomatic at 9 months compared to 23% and 24% respectively in the non sphincter tear group. In contrast Haadem et al. 1988 found no improvement in symptoms at 5 and 9 month intervals in women with clinically diagnosed sphincter tears. Zetterstrom et al. 1999 hypothesised the symptomatic improvement seen in the sphincter tear group to be due to spontaneous normalisation of pudendal nerve latencies following delivery, compensatory function in maintaining continence by puborectalis and the pelvic floor musculature and the reinnervation of pelvic floor oestrogen receptors following termination of breast feeding (Zetterstrom et al. 1999).

There has also been some inconsistency within the literature regarding the long term outcome of anorectal function following obstetric anal sphincter injury. De Leeuw et al. 2001 analysed postal questionnaire responses sent to 125 women with a history of third or fourth degree tears at a median follow up of 14 years. Thirty one percent of women were incontinent at 14 year follow up with the severity of symptoms being greater and starting sooner after delivery in comparison to the control group. Pollack et al. 2004 reported a 53% prevalence of faecal incontinence in primiparous women at 5 year follow up in keeping with previous studies (Sultan et al. 1994; Tetzschner et al. 1996; Haadem et al. 1988; Poen et al. 1998). This evidence allows one to speculate that the trauma sustained during vaginal deliveries may not present itself until many years later due to the compounding effects of aging, menopause and progression of neuropathy (Sultan et al. 1993; Tjandra et al. 2008).

At present it still remains unclear as to what the natural history of anal sphincter tears is, although it is now evident that the mechanism of injury varies between first and subsequent deliveries. There is some evidence that women who have sustained an obstetric anal sphincter tear with their first born may experience a deterioration of their incontinence symptoms following subsequent vaginal deliveries (Bek and Laurberg 1992; Sangalli et al. 2000; Poen et al. 1998). Reasons for this observation include repeated injury or increased severity of injury of the anal sphincter during a second delivery along with the effect of cumulative stretching of the pudendal nerve and pelvic

floor musculature following multiple vaginal births. In contrast to these findings, De Leeuw et al. 2001 found no association between subsequent vaginal delivery and development of faecal incontinence. A possible explanation for this may be due to the high use of mediolateral episiotomy in the study carried out by De Leeuw et al. 2001 compared to the use of midline episiotomies in other studies which may carry a better functional prognosis. One important factor limiting accurate comparison between studies is the use of mixed parity women. Fynes et al. 1999 removed the confounding factor of mixed parity by prospectively following 59 nulliparous women through two successive vaginal deliveries. Of the 20 women that had evidence of sphincter defects on endoanal ultrasonography after first vaginal delivery; 13 were symptomatic and 7 were asymptomatic. Of the 13 women who were symptomatic following their first delivery; 8 remained persistently symptomatic during their second pregnancy, and of these, 7 reported further deterioration in faecal continence following their second vaginal delivery. All of the remaining 5 women who were initially symptomatic following their first delivery had resolution of their symptoms during the second pregnancies, but 2 women became symptomatic again following their second delivery. Three out of five women with an occult sphincter injury at first vaginal delivery developed symptoms for the first time after their second vaginal delivery. The authors concluded that women with transient faecal incontinence, occult anal sphincter injury or persistent faecal incontinence symptoms during their second pregnancies are at high risk of deterioration of symptoms after second vaginal delivery.

1.8 Pelvic floor injury

Although the risk factors and consequences associated with obstetric anal sphincter injury have been extensively described, puborectalis trauma has received less attention. Levator ani avulsion defects occur in 15-35% of parous women delivering vaginally (Dietz 2007). Whilst levator avulsions are associated with pelvic organ prolapse a clear correlation with incontinence remains to be established. This may occur because patients with a traumatised puborectalis maintain continence through preserved distal anal sphincter function, compensating for the loss of the proximal component. Other forms of injury to the levator ani muscle have also been objectively visualised and documented with the use of MRI and 3D transperineal ultrasound and include stretching or distension injury, partial or total detachment of the pubovisceral sling from the pubic bone and neurological injury resulting in decreased levator ani muscle strength (Snooks

et al. 1986; Allen et al. 1990; Dietz et al. 2008; Valsky et al. 2009; Delancey et al. 2003). It has become clear that vaginal childbirth particularly in parous women is the single most important risk factor in the development of pelvic floor dysfunction with the assumption that such defects commonly result during crowning of the foetal head (DeLancey et al. 2003; Kirschner-Hermanns et al. 1997; Tunn et al. 1998; Dietz et al. 2005; Mant et al. 1997; Skoner et al. 1994; Viktrup et al. 1992).

1.8.1 Risk factors of pelvic floor injury

Very few studies to date have investigated the obstetric factors relating to levator ani muscle injury following vaginal birth. Kearney et al. 2006 reported increased odds ratios for levator defect with forceps use (OR 14.7), anal sphincter rupture (OR 8.1) and episiotomy (OR 3.1) in 160 primiparous women. They also found that the women who sustained levator trauma were significantly older (3.5 years p=0.001) and had a longer duration of second stage (78 minutes p=0.001). In support of this, Gainey 1943 and 1955 and Ranney 1990 have both shown a reduction in levator injury and subsequent development of pelvic organ prolapse in conjunction with using an early generous mediolateral episiotomy. The use of forceps with episiotomy was reported to result in a 3 fold reduction in levator injury (Gainey 1943 and 1955). More recently, Valsky et al. 2009 prospectively evaluated the potential risk factors and rate of levator avulsion trauma using 3D transperineal ultrasound 24-72 hours post delivery in 210 primiparae and a control group consisting of 32 nulliparae and 15 primiparous women delivered by elective caesarean section. In the study group 39 (18.6%) women sustained a sonographic levator ani defect with no defects seen in the control group. This finding implies that elective caesarean delivery plays an important role in the protection against levator ani muscle avulsion injury. Of the risk factors, foetal head circumference, foetal birth weight and duration of second stage of labour were significantly associated with levator injury. Following logistic regression analysis, foetal head circumference ≥35.5cm and second stage duration ≥110 minutes increased the odds of sustaining levator trauma by a factor of 5.32 (Valsky et al. 2009). Interestingly, episiotomy was found to have a protective effect on the levator ani muscle. The authors hypothesised that incising the mediolateral part of the pubovisceral sling results in a decrease in pelvic floor distension during crowning of the foetal head resulting in a reduced risk of levator ani avulsion (Valsky et al. 2009). Further larger long term prospective trials are essential in identifying women at greatest risk of pelvic floor injury during vaginal

childbirth and modifying obstetric factors which can potentially lead to pelvic floor dysfunction (Valsky et al. 2009).

1.9 Pudendal nerve injury

Pudendal nerve damage secondary to vaginal delivery has been speculated as a key aetiological factor in the subsequent development of faecal incontinence, stress urinary incontinence and genital tract prolapse, historically being regarded as more important than muscular disruption (Parks and Swash 1977). Such pudendal neuropathy is biologically plausible given the anatomy of structures around the birth canal and the tortuous course of the nerve within the pelvis, and indeed many studies have demonstrated pudendal nerve dysfunction in women following vaginal delivery and those with pelvic floor dysfunction (Snooks et al. 1986; Allen et al. 1990; Sultan et al. 1994). The exact mechanisms of nerve injury are uncertain but abnormal perineal descent, traction injury during elongation of the birth canal and at the level of the ischial spine along with compression of the nerve in Alcock's canal during descent of the foetal head in the second stage of labour or direct avulsion of the terminal fibres during instrumental delivery have all been implicated (Fitzpatrick and et al. 2003).

Pudendal nerve injury has been quantified in the past by the use of EMG & PNTML (to be discussed in chapter 2), however, the clinical relevance of these tests remains controversial. The introduction of anal endosonography in the early 1990's has revolutionised our understanding of the pathogenesis of faecal incontinence secondary to obstetrical anal sphincter injury along with its investigation and management (Law et al. 1991; Kamm 1994). The aetiology was previously believed to be primarily due to pudendal neuropathy but EAUS has now shown that mechanical sphincter trauma is the commonest aetiological factor (Sultan et al. 1993).

1.10 Assessment

Ideally assessment of obstetric related anal sphincter injury should take place in a dedicated multidisciplinary perineal clinic 6-8 weeks post delivery where a thorough history is elicited and clinical examination is performed. Subsequently, anorectal physiology testing and endoanal ultrasound of the anal sphincter complex should be performed allowing assessment of neuromuscular function of the sphincters and anal anatomical integrity. Recently, external phased MRI and endoanal MRI (which is

discussed in chapter 2) have been proven to be excellent techniques in the accurate detection of anal sphincter atrophy.

1.10.1 Anorectal Physiology

Anorectal manometry can take many forms and is a widely available technique used to obtain selected information concerning anorectal function in patients with faecal incontinence. Resting anal pressure results from continuous rhythmical slow wave activity of the internal anal sphincter and the tonic activity of the external anal sphincter. Squeeze pressure is caused by contraction of the external anal sphincter. Hence, defects of the external sphincter are associated with significantly lower squeeze pressure increments and defects of the internal sphincter are associated with lower resting pressures (Sultan et al. 1993). Studies have demonstrated external anal sphincter bulk to correlate strongly with squeeze increment (Williams et al. 2001).

Rectal hypersensitivity defined as a reduced sensory threshold to volumetric rectal distension is common in those with faecal urgency with either a normally functioning or dysfunctional external anal sphincter (Yeoh et al. 2004; Chan et al. 2005; Loening-Baucke et al. 1989). Anorectal sensory testing using an electrical stimulus is the simplest way to obtain a quantitative guide to anorectal innervation. At present, it is not of established value for the diagnosis and treatment of patients with incontinence, except when it is necessary to distinguish an idiopathic or functional disorder from a primary disorder or from a secondary disorder affecting extrinsic or intrinsic nerves e.g. diabetes mellitus (AGA review 1999).

1.10.2 Endoanal Ultrasound (to be discussed in more detail in chapter 2)

Abnormalities of structural integrity of the anal sphincter complex can be identified with this technique, as can more subtle abnormalities of internal sphincter smooth muscle texture and composition (Kamm 1994). The procedure is simple, rapid, widely available and without radiation exposure. Although interpretation is operator dependent, in the hands of experienced operators sensitivity and specificity approaches 100% (Felt-Bersma et al. 1995; Law et al. 1990; Burnett et al. 1991; Felt-Bersma et al. 1992; Sultan et al. 1994). Close correlation between endosonographic images and anatomical structures have been demonstrated by in vitro, in vivo and physiological studies (Sultan et al. 1993 and 1994).

The hypoechoic internal anal sphincter is a dense ring of smooth muscle with a high water content and is easily recognisable from the mixed echogenicity of the external anal sphincter (figure 1.1) and the u shaped hyperechoic sling of the puborectalis muscle (figure 1.2).

Figure 1.1 Endoanal ultrasound at mid anal canal level demonstrating the appearances of normal intact external anal sphincter (black arrow) and internal anal sphincter (white arrow)

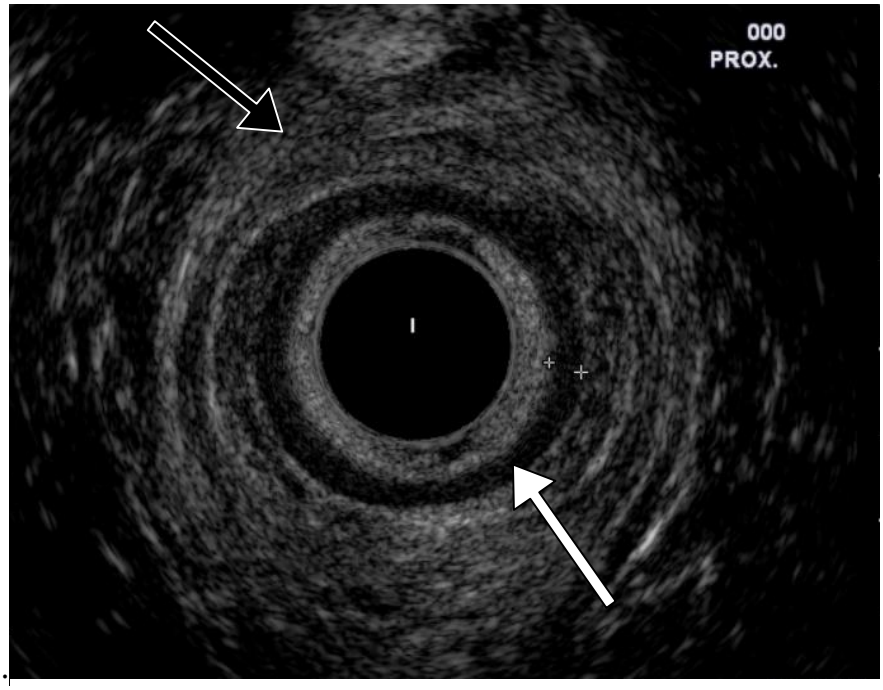
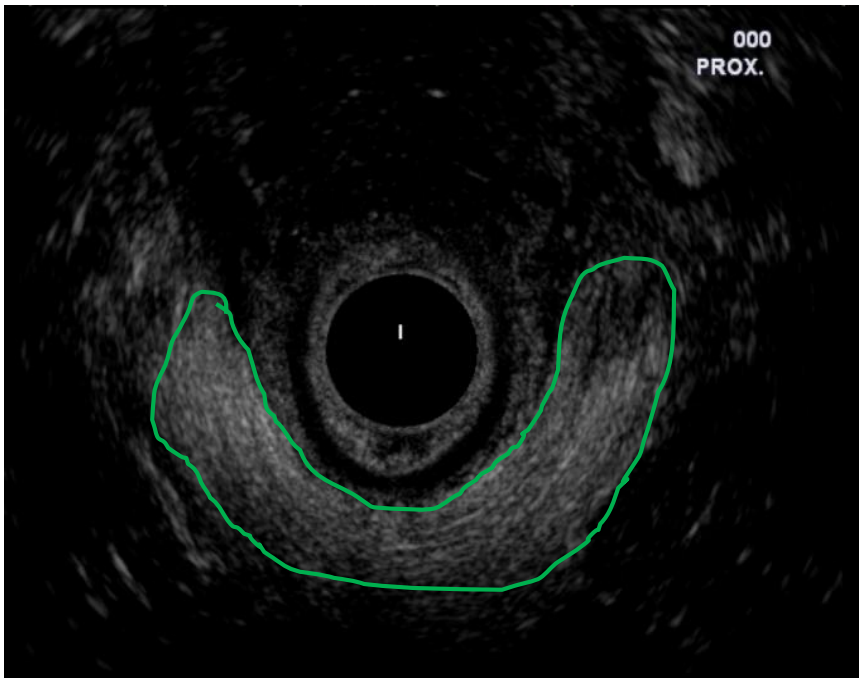


Figure 1.2 Endoanal ultrasound at upper anal canal level demonstrating normal appearances of puborectalis muscle (outlined).



EAUS has a complementary role to anorectal manometry and is important in linking different symptoms of incontinence with differing muscle pathologies. Passive faecal incontinence is typically associated with primary degeneration of the internal anal sphincter occurring with degenerative diseases such as systemic sclerosis, incisional surgery such as lateral sphincterotomy or fistulotomy and dilatation procedures. Faecal urgency or urge incontinence is typically associated with external sphincter dysfunction most commonly resulting from obstetric trauma. Idiopathic faecal incontinence secondary to external sphincter denervation is reported to lead to thinning of the external sphincter muscle and thickening of the internal sphincter muscle (deSouza et al. 1995; Emblem et al. 1994).

1.10.3 Puborectalis function assessment

Due to the close anatomical proximity of the puborectalis and external anal sphincter, it remains to be determined how current physiological measures can accurately discriminate between the two structures. An additional difficulty in understanding the role of puborectalis function has arisen due to the absence of a standardised measurement technique. So far, MRI has been proposed for accurate anatomical imaging (Gousse et al. 2000) whilst various types of devices and techniques (perineal

dynamometer, water or air filled balloon, vaginal cone and vaginal mould) have been described in the past as methods for physiological assessment of puborectalis muscle strength in the form of measuring vaginal pressure (Hahn 1996; Dougherty et al. 1986; Bo 1992). Theoretically the vagina lacks an intrinsic sphincter mechanism and hence it has been speculated that the vaginal high pressure zone is reflective of pelvic floor muscle contraction (Guaderrama et al. 2005). The problems associated with the earlier developed measurement techniques are that firstly they fail to measure absolute pressure and secondly they measure an average pressure along the whole length of the vagina rather than dividing the vagina into different segments or pressure zones.

An American group led by Mittal have been the first and only collaborative to describe the composite vaginal pressure profile at rest and during squeeze using side hole water infused vaginal manometry and motorised pull through in 14 nulliparous controls (Guaderrama et al. 2005). They reported that the vagina did not contain a uniform pressure area but one with three different pressure zones; proximal, mid and distal (Guaderrama et al 2005). The highest pressures were recorded in the anteroposterior direction in the mid zone or vaginal high pressure zone which was 3-4 cm long with a peak pressure approximately 2cm superior to the vaginal hymen. This study did not look at which component of the levator ani muscle contributed to the high pressure zone or the anatomic correlates of the three pressure zones however it was hypothesised that the puborectalis muscle is responsible for generating the vaginal high pressure zone along with the proximal pressure zone reflecting intra abdominal pressure, the mid pressure zone reflecting pelvic floor muscle contraction and the distal pressure zone reflecting atmospheric pressure (Guaderrama et al. 2005).

Following on from this work the same group performed a further study to determine the functional correlates of anal canal anatomy and to understand the contribution of puborectalis to the genesis of anal canal pressure using simultaneous 3D endovaginal ultrasonography and water perfused anal manometry in 17 nulliparous controls (Liu et al. 2006). They reported an increase in anal canal pressure during voluntary squeeze in both the proximal and distal parts of the anal canal which anatomically correlated with the puborectalis muscle and external anal sphincter respectively on 3D ultrasound. They also observed circumferential asymmetry of anal canal pressures in the proximal part of the anal canal (puborectalis muscle zone) and more symmetrical pressures being

generated in the distal part of the anal canal (external anal sphincter zone) which can be explained by the u-shaped puborectalis and circular shaped external anal sphincter. This study demonstrates the important role that puborectalis plays in the maintenance of faecal continence and that faecal incontinence secondary to anal sphincter dysfunction may be not only due to disruption of the internal and/or external sphincter but also due to puborectalis disruption. This observation may also explain the poor outcome of secondary surgical external anal sphincter repair when ultimately there may be a puborectalis muscle disruption or tear which is the root of the problem and is not appropriately addressed. Further studies are required to investigate the effects of anatomic disruption of the anal sphincter complex on function.

1.11 Conclusion

In summary, the incidence of obstetric anal sphincter tears is influenced by a complex interplay of obstetric, maternal and foetal risk factors. Further work is required to firstly, clarify the association between anal sphincter and pelvic floor anatomy, physiology and symptoms of faecal incontinence; and secondly to review the relationship between the better quantifiable mechanical factors and the less well quantified neurological factors. During this thesis I will be focussing on some of these missing areas discussed by carrying out a series of interlinking studies.

I will be primarily looking at quantifying puborectalis muscle and external anal sphincter structure and puborectalis muscle function; firstly by using vaginal manometry as a possible complementary or better measure of puborectalis muscle function in comparison to anorectal manometry (chapter 4) and secondly, by using specific magnetic resonance imaging techniques to look at the anatomical structure of puborectalis and external anal sphincter (chapter 5). However, before this I will be quantifying the characteristics of our study cohort (chapter 3) in addition to discussing the physiological changes that can occur, specifically atrophy, of the anal sphincter musculature.

CHAPTER TWO

ATROPHY OF THE ANAL SPHINCTER COMPLEX

2.1 Introduction

Muscular atrophy is a consequence of sphincteric injury which is initially occult in nature as opposed to clinically overt. A substantial proportion of women with an occult sphincter injury will develop incontinence symptoms later in middle age as a result of the cumulative effect of subsequent deliveries, the effect of ageing, declining oestrogenic support of the pelvic floor connective tissue after the menopause or progression of neuropathy and anal sphincter atrophy (Sultan et al. 1993).

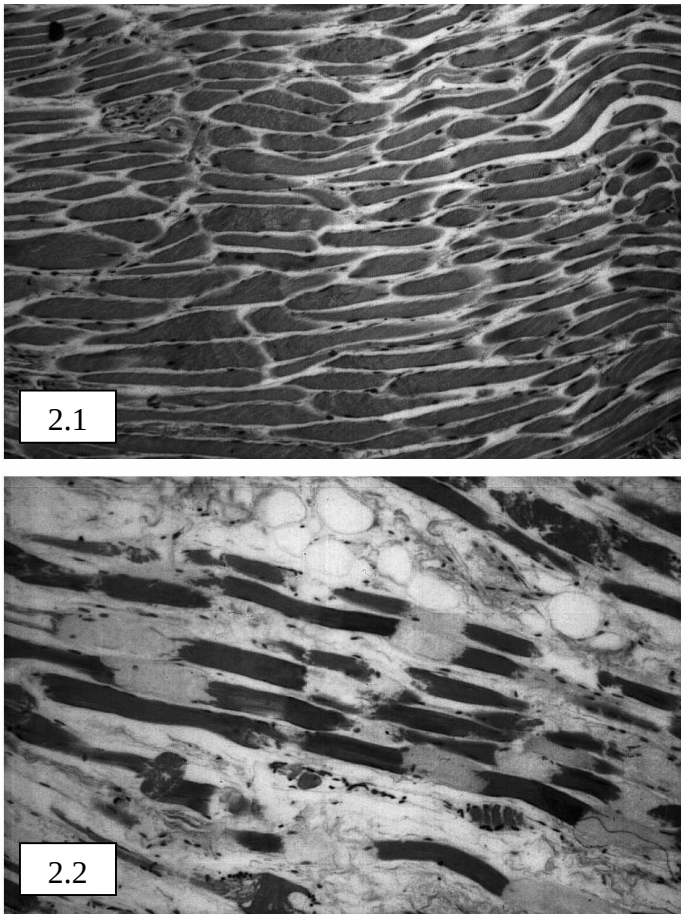
This chapter will review the history, development and current evidence regarding the investigations and imaging modalities used in the assessment of the anatomic and pathologic characteristics namely atrophy of the anal sphincter muscles.

2.2 Definition, types and process of atrophy

Muscle atrophy is defined as a decrease in muscle mass secondary to lack of use or neurogenic dysfunction. More specifically, EAS atrophy is considered to be the result of denervation injury and has been demonstrated in patients with neurogenic idiopathic faecal incontinence (Swash 1983). Factors influencing the end effects of denervation on the striated EAS muscle include axonal distribution, degree and duration of nerve damage. Following denervation, individual muscle fibres are either reinnervated from branching of adjacent surviving axons or undergo degeneration and atrophy with fatty replacement (Williams et al. 2001). In particular, atrophy of the EAS is characterised by extreme thinning of the muscle fibres and/or generalised fatty infiltration (Briel et al. 2000, figures 2.1 and 2.2). Reinnervated muscle fibres show recognisable histological changes with an increase in the mean number of muscle fibres supplied within a single motor unit (Williams et al. 2001). In comparison, denervated muscle results in a loss of the normal mosaic pattern of type 1 and type 2 fibres secondary to fibre type grouping as well as muscle fibre loss with fat and fibrous tissue replacement (Parks et al. 1977; Williams et al. 2001).

Figure 2.1 Biopsy specimen of normal external anal sphincter (Briel et al. 2000)

Figure 2.2 Biopsy specimen of atrophied external anal sphincter (Briel et al. 2000)



2.3 Causes of atrophy and tests detecting denervation injury

Pudendal nerve injury secondary to childbirth is now known to be an important component to the subsequent development of FI amongst women. Parks et al. 1977 were the first to describe neurogenic faecal incontinence due to denervation of the anal sphincter muscle complex as a result of pudendal nerve compression or stretch injury secondary to childbirth injuries or rectal descent caused by repetitive straining defecation in constipated patients. Up until recently, the condition of the EAS and the presence of muscle atrophy secondary to pudendal neuropathy could only be assessed and quantified by pudendal nerve terminal motor latencies (PNTML) and electromyography (EMG) (Stoker et al. 2000).

2.4 Pudendal nerve terminal motor latency

Motor latency is defined as the time measured from stimulation of a motor nerve to the muscle response. More specifically, PNTML is determined by recording anal sphincter

muscle action potentials evoked by stimulation of the pudendal nerve near the ischial spine through the rectal wall (Lefaucher 2006). Prolonged nerve conduction indicates injury to the pudendal nerve sheath resulting in focal demyelination and slowing of conduction. This technique was developed by Kiff and Swash in 1984 based on an electro-ejaculation procedure. This was followed by Rogers et al. 1988 who designed a disposable pudendal nerve bipolar stimulator the 'St Marks Electrode' consisting of stimulating and recording electrodes that could be glued and mounted onto the index finger of a gloved hand. Insertion of the St Marks Electrode into the rectum allows measurement of PNTML (figures 2.3 and 2.4) by stimulating the pudendal nerve at the tip of the finger and recording the anal motor responses at the base.

Figure 2.3 Normal PNTML trace

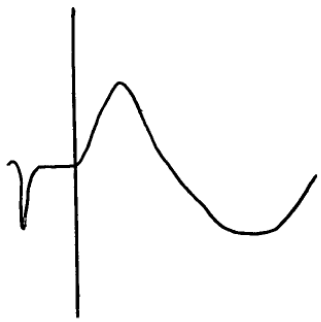
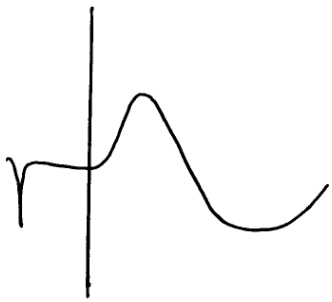


Figure 2.4 Prolonged PNTML trace



It is now clear that PNTML only reflects the conduction velocity of the fastest motor nerve fibre supplying the anal sphincter (Lubowski et al. 1988) and hence is only abnormal when the largest and most heavily myelinated nerves are damaged and remain injured. In addition the PNTML may be normal even in the presence of EAS atrophy,

therefore suggesting PNTML testing may not detect evidence of subtle focal peripheral nerve injury, past injury or atrophy. In the past, clinicians quantified nerve injury with PNMTL in women with symptomatic pelvic floor dysfunction such as faecal incontinence, urinary incontinence or pelvic organ prolapse secondary to childbirth. However, the clinical relevance of this electrophysiological test remains controversial with many colorectal surgeons, gastroenterologists, urogynaecologists and neurophysiologists relying less frequently on this test. The American Gastroenterological Association does not advise use of the test for work up and evaluation of patients with faecal incontinence (Barnett et al. 1999). Despite this, many centres still continue to use PNTML and anorectal manometry to assess individuals with faecal incontinence.

In theory, pudendal nerve latency, EMG interference pattern and squeeze pressure should be directly associated as the pudendal nerve directly affects voluntary contraction of the external anal sphincter. However many recent studies have failed to show that this test has adequate sensitivity and specificity. There is poor or no correlation between pudendal nerve latencies and squeeze pressures (Thomas et al. 2002; Hill et al. 1994; Tetzschner et al. 1995; Vaccaro et al. 1995; Osterberg et al. 2000; Rasmussen et al. 2000; Suilleabhain et al. 2001) or symptoms (Vaizey et al. 1999; Riciardi et al. 2006). In comparison, concentric needle EMG has been reported to show better diagnostic sensitivity and correlation between symptoms and anal manometry than PNTML measurement (Barnett et al. 1999; Wexner et al. 1991; Cheong et al. 1995; Thomas et al. 2002; Strijers et al 1989). One must also remember that before software to calculate the latency was developed, earlier studies placed the marks for latency calculation by hand, and so, were prone to error. Further limitations of this test include poor reproducibility, unknown validity, need for reliable equipment and availability of an experienced operator. The exact positioning of the electrodes, stimulus strength, and manual determination of response latency, are also all open to personal bias.

2.5 Electromyography

Electromyography (EMG) of the external anal sphincter is performed for three purposes: 1) to identify the presence of sphincter injury, 2) to determine contraction or relaxation of the muscle, and 3) to identify denervation-reinnervation potentials indicative of nerve injury (Barnett et al. 1990). The two classic EMG methods are that

of single-fibre EMG and concentric needle EMG. Concentric needle EMG uses a disposable electrode and typically samples all four quadrants of the EAS therefore allowing a large number of motor units to be sampled simultaneously. A muscle motor unit comprises a single nerve cell, its axon and the skeletal muscle fibres it supplies. The needle electrode located near the EAS muscle fibres detects the summated electrical potentials and displays it as a wave form called a motor unit action potential (MUAP). Additional information provided and analysed include spontaneous activities, MUAP morphology and MUAP recruitment during voluntary or reflex contraction i.e. cough or perineal skin pinching (Lefaucheur 2006).

Single-fibre EMG is used to demonstrate fibre density which is defined as the mean number of muscle fibres present in a single motor unit per sampling site. The normal fibre density for the EAS is below 2.0 and an increase in its value results from collateral reinnervation secondary to neuropathic injury. Up until relatively recently, single fibre EMG was thought to be the gold standard for the diagnosis of pudendal nerve dysfunction and subsequent anal sphincter denervation and atrophy. However, its use is limited clinically due to unrepresentative sampling of the sphincter, patient discomfort and liability to sampling error (Williams et al. 2001). Secondly, the relationship between EMG values and physiological variables such as age, gender, temperature and muscle fibre composition, length, fibre diameter and firing frequency are yet to be confirmed hence limiting the value of EMG (Arendt-Neilsen and Zwarts 1989).

2.6 Endoanal Ultrasound

Needle electromyography (EMG) has been used in the past to map anal sphincter defects however the invasiveness of the technique with multiple needle insertions has limited its use in the clinical setting (Stoker et al. 2000). The introduction of endoanal ultrasonography (EAUS) since the early 1990s has afforded clinicians improved ability to identify structural defects in the anal sphincter complex and has revolutionised our understanding of the pathogenesis of faecal incontinence, along with its investigation and management (Law et al. 1991; Kamm 1994). It also has the added advantage of being an accurate, painless alternative to needle EMG (Law et al. 1991; Felt-Bersma et al. 1992; Tjandra et al. 1993; Enck et al. 1996). The technique has been validated histologically (Sultan et al. 1994), intraoperatively (Sultan et al. 1993) and physiologically (Sultan et al. 1993). Prior to its introduction the integrity of the anal

sphincter complex was exclusively dependent on the poorly validated technique of digital examination.

Two dimensional (2D) EAUS is the conventional imaging modality used to define the anatomy of the anal sphincter complex. This technique is optimal for evaluation of internal anal sphincter anatomy due to the differentiation of the hypoechogenic smooth muscle from the echogenic subepithelial tissues medially and the longitudinal muscle laterally (Malouf et al. 2000). In contrast the visualisation of the external anal sphincter (EAS) can be difficult due to the mixed and variable echogenicity of the muscle making the muscle boundaries more difficult to define (Malouf et al 2000). Assessment of the condition of the sphincter muscle is crucial in the selection of patients with a sphincter defect for surgery. Sphincter atrophy has been shown to be associated with poor outcome following sphincter repair (Briel et al. 1999; Briel et al. 2000).

Three dimensional (3D) EAUS has recently overtaken the role of conventional 2D EAUS in the assessment of anal sphincters with the benefit of providing multiplanar imaging of the anal canal thereby enabling reconstruction of axial images in the coronal and sagittal planes. Unlike conventional EAUS, 3D EAUS produces a digital volume that may be used to perform measurements in any plane and therefore provide more reliable information on the anal sphincter complex and accompanying defects in faecally incontinent subjects (West et al. 2005). Another advantage of 3D imaging is the ability to review the entire dataset of paired examinations once the volume of data has been acquired (Williams et al. 2001). The advantages of EAUS per se is that it is simple, rapid, widely available and does not expose the patient to radiation. Whilst interpretation is operator dependent, in the hands of experienced operators sensitivity and specificity approaches 100% (Felt-Bersma et al. 1995; Law et al. 1990; Burnett et al. 1991; Felt-Bersma et al. 1992; Sultan et al. 1994).

Although EAUS has been shown to be a more sensitive tool in depicting structural defects of the EAS in comparison to endoanal MRI (deSouza et al. 1996; deSouza et al. 1995; Rociu et al. 1999; Dobben et al. 2007), the condition of the EAS is better visualised with endoanal MRI. The high intrinsic contrast and high spatial resolution provided by endoanal MR imaging accurately shows the difference in contrast between the EAS muscle and surrounding fat, thereby enabling more precise demonstration of

normal sphincter anatomy and pathologic conditions such as muscle tears, abscesses, fistulous tracks, scars, atrophy and hypertrophy (Dobben et al. 2007; Cuesta et al. 1992). Several studies have compared EAUS and endoanal MRI for detecting EAS defects and have shown differing results. Malouf et al. 2000 in a single centre prospective study showed poor interobserver agreement (62% of subjects) between endoanal MRI and EAUS in the detection of sphincter defects. In contrast, Dobben et al. 2007 reported no significant difference between MR imaging and USS in the detection of sphincter defects which was confirmed in 86% of subjects (31 of 36) who underwent surgical anal sphincter repair. This difference in results may reflect more recent improvements in technology along with a greater understanding of the EAS anatomy on EAUS and MRI.

2.7 Magnetic resonance imaging and external anal sphincter atrophy

Imaging has recently taken a central role in the assessment of patients with faecal incontinence, with endoanal or endocoil MRI being proved to be an excellent tool for the detection of anal sphincter atrophy (West et al. 2005) rendering EMG and assessment of PNTML largely redundant (Briel et al. 2000).

Aronson et al. 1990 were the first to describe the anatomy of the anal sphincters with MRI in the early 1990s on 5 faecally continent nulliparas of reproductive age. They concluded soft tissue differentiation on MRI to be superior to that of sonography and computer tomography (Aronson et al. 1990). Since then MR studies of the anorectal region using a surface or body coil have been shown to produce poor resolution and visualisation of the different muscle layers (Aronson et al. 1990; Myhr et al. 1994; Lunniss et al. 1992; Schafer et al. 1994). MR imaging of the anal sphincter complex with a dedicated endoanal coil was first introduced in 1995 (Aronson et al. 1990; deSouza et al. 1995) and has since been utilised in the diagnostic workup of patients with faecal incontinence (Briel et al. 2000; deSouza et al. 1995; Hussain et al. 1995; Stoker et al. 1996). The close positioning of an endoanal coil to the sphincter generates a 10 fold increase in the signal-to-noise ratio at the anal sphincter producing higher spatial resolution. In addition, the differing signal intensities of MRI between the internal and external sphincters and the ability to image in multiple planes are of considerable value in the visualisation of the normal anatomy and pathological conditions of the anal sphincter complex. The internal anal sphincter is better defined

with endosonography due to its hypoechoic structure contrasting against hyperechoic adjacent tissues. In contrast, the low signal intensity of the external anal sphincter is clearly highlighted against the high signal intensity of the perianal fat laterally and the intersphincteric fat medially with MR imaging (deSouza et al. 1996).

Although some studies have shown both endosonography and MR as accurate imaging modalities in depicting structural defects of the EAS and others just MR, one definite area in which endocoil MR imaging is superior is in the detection of external anal sphincter atrophy (Bartram 2005; Briel et al. 1999; deSouza et al. 1995; Rociu et al. 1999; Williams et al. 2001; Rocui et al. 1999; deSouza et al. 1996; Briel et al. 2000; Fletcher et al. 2003; Stoker et al. 1996; Stoker et al. 1999; Stoker et al. 2002; Enck et al. 1997; Rocui et al. 2000). Atrophy and thinning of the EAS cannot be demonstrated with conventional EAUS due to the poor intrinsic contrast leading to inaccurate identification and measurements of the EAS muscle diameter being made (Briel et al 2000;Enck et al. 1997). However, the high intrinsic contrast of endoanal MRI and the availability of the oblique coronal plane allows the diameter of all anal muscles to be compared making atrophy easier to detect (Rociu et al. 1999).

Briel et al. 2000 have been the only group to compare the morphology of the EAS on endocoil MRI, in particular atrophy, to the gold standard of histological examination. Endocoil MRI correctly identified normal and abnormal sphincter morphology in 23 of 25 cases (92%). The prevalence of sphincter atrophy was 36% (9 of 25 cases) identified by MRI, with confirmation in all but one from histopathological investigation. All study participants were faecally incontinent secondary to obstetric trauma, in addition to the primary study findings, no relationship between EAS atrophy and patient's age was found, neither was there any difference between the prevalence of sphincter atrophy in patients with immediate or late onset faecal incontinence. One can therefore conclude that denervation of the pelvic floor as a result of obstetric trauma is primarily responsible for sphincter atrophy rather than aging of the patient and the effects of menopause.

2.8 Why measure atrophy

In patients with faecal incontinence secondary to a sphincter defect, visualisation of the sphincter enables exact analysis of the defect, its position and condition of the remaining sphincter muscle and hence ensures selection of the correct patient who may benefit from surgical repair. There is evidence linking pudendal neuropathy and

subsequent atrophy of the EAS with poor outcome from EAS surgical repair (Roig et al. 1995; Henry 1994; Parks et al. 1977; Engel et al. 1994; Felt-Bersma et al. 1996; Simmang et al. 1994; Birnbaum et al. 1996; Pinta et al. 2003). This highlights the clinical importance of detection of EAS atrophy in faecally incontinent patients which should be used as a guide for adequate patient selection for surgical repair. Briel et al. 1999 looked at the impact of EAS atrophy on outcome of sphincteroplasty in 20 women with faecal incontinence secondary to obstetric trauma. Continence was restored in 13 of the 20 patients with 8 of the 20 patients having EAS atrophy. There was a significant improvement in outcome in subjects without EAS atrophy (11 of 12 vs 2 of 8). In addition Briel et al. 1999 were the first to measure sphincter bulk in relation to outcome for sphincter repair. They demonstrated that 3 out of 10 patients with an EAS sphincter area of 360mm^2 or less measured in the midcanal on an axial image had a successful outcome post surgical repair compared with all 10 patients with a sphincter area of greater than 360mm^2, confirming that thin atrophic sphincters have a negative predictive value for good outcome (Briel et al. 1999; Bartram 2005).

This work was followed up by Williams et al. 2001 who looked at the role of endocoil MRI in the quantification of EAS atrophy relating to single fibre EMG recordings along with validating a visual grading system of EAS atrophy. They demonstrated a significant correlation between grade of atrophy and squeeze pressure, sphincter area and mean fibre density. Of the 25 women taking part in the study, the EAS was graded on a midcoronal image as normal i.e. well defined muscle bulk with low fat content in nine women, intermediate i.e. preserved sphincter bulk with increased fat content in eight women and advanced i.e. reduced muscle bulk with increased fat content in eight women; which was validated with known morphological differences of EAS atrophy and confirmed with direct EMG. Successful EMG assessment was undertaken in eleven women, of which eight were in the normal group, two in the intermediate group and one in the advanced group. Inability to record electromyographic activity from the EAS was associated with atrophy of the EAS as demonstrated on MRI. In addition, Williams et al. 2001 reported EAS atrophy on MRI in women in whom no electromyographic potential was recorded from one side of the sphincter supporting the advantage of imaging and assessing the entire anal sphincter. They concluded that endocoil MRI should be considered for assessing muscle quality prior to anal sphincter surgery.

2.9 Surface bodycoil versus endocoil MRI in detecting atrophy

Although MRI offers many advantages for studying the anorectal musculature including no requirement of preparation or contrast medium, no utilisation of ionising radiation and lack of operator dependence, it has limitations. The main disadvantages of MR imaging with an endoanal coil compared with endosonography are the cost and the time taken to perform the investigation. In addition, the introduction of an endoanal coil causes patient discomfort and the use of endoanal MRI is restricted to specialised centres as the endoanal coil is not widely available with every MR machine. The limited length of the endoanal coil resulting in limited length of view of the surrounding anatomy of the anal canal secondary to the signal to noise drop off with distance from the coil has also been noted to be a limiting factor in the evaluation of the extent of anorectal tumours (deSouza et al. 1996; Beets-Tan et al. 1999).

These disadvantages have since been verified with the introduction of external or surface phased array coils which increase the signal to noise ratio therefore allowing high resolution images to be obtained (Beets-Tan et al. 1999). Studies have shown that MRI of the anorectal region with an external phased array coil is feasible and produces detailed views of the anatomy of the anal sphincter and surrounding structures (Morren et al. 2001; Beets-Tan et al. 2001) and identified useful applications in the assessment of the presence and extent of anorectal defects and anorectal disease such as anorectal fistulas, faecal incontinence and anorectal tumours (Beets-Tan et al. 1999:Terra et al. 2006; Beets-Tan et al. 2001; deSouza et al. 1998; Terra et al. 2005). In the evaluation of atrophy, Terra et al. 2006 are the first and only group to compare external phased array MRI to endoanal MRI in depicting EAS atrophy in patients with faecal incontinence. They reported good agreement (k=0.72) between both MRI techniques in depicting atrophy. The authors also found a weak interobserver agreement and stronger intraobserver agreement depending on the level of experience of each of the 3 observers leading to the conclusion that both forms of MR imaging were recommended in the diagnostic workup of patients with faecal incontinence as long as sufficient experience was available (Terra et al. 2006). Quantitative measurements of atrophied external anal sphincters were found to be smaller with both techniques. However, overall EAS thickness was significantly smaller with endoanal MR imaging compared to external phased array MR imaging; the authors explained this discrepancy by stretching of the anal sphincter muscles leading to smaller thickness measurements being made with the

introduction of an endocoil device. Limitations of this study include small sample size leading to poor study power, lack of validation of EAS atrophy to histology as the gold standard and finally the use of subjective qualitative interpretation of atrophy with no established atrophy scoring criteria.

2.10 3-dimensional EAUS versus MRI in depicting atrophy

The wide availability of 3D EAUS has recently raised the question of its use in the detection of EAS atrophy. It is thought that although EAUS cannot detect fatty infiltration, certain sphincter measurements made using 3D EAUS may be able to predict the presence of EAS atrophy compared to conventional 2D EAUS (West et al. 2005). Williams et al. 2002 used a graphics overlay technique to directly compare thickness of the main anal canal layers between axial endocoil MRI and 3D EAUS images at the same level in 9 healthy subjects. They reported that despite poorer sonographic definition of the EAS there was still an excellent correlation and interobserver agreement in the measurement of its thickness with endoanal MRI suggesting its use in the depiction of EAS atrophy. West et al. 2005 in a study of 18 faecally incontinent women all with evidence of EAS atrophy on endoanal MRI found very poor correlation between 3D EAUS and endoanal MRI for EAS thickness, area and length. Furthermore 3D EAUS produces a digital volume allowing measurements in any plane to be performed theoretically providing parameters for detecting atrophy, however, West et al. 2005 failed to show any correlation between EAS volume measured on 3D EAUS and EAS thickness and area measured on endoanal MRI. One possible explanation of this discrepancy may be due to the loss of contrast between the outer border of the atrophied EAS and the adjacent ischio-anal fat. The authors did not compare inter and intraobserver agreement for 3D EAUS and endoanal MRI measurements in this study however previous work carried out by them showed no inter or intraobserver variability in EAS volume, length and thickness using 3D EAUS in healthy subjects (West et al. 2005). Most recently, Cazemier et al. 2006 reported good agreement between 3D EAUS and endoanal MRI in 83% of patients in the detection of EAS atrophy indicating the use of 3D EAUS as a diagnostic tool for EAS atrophy. However, the authors found poor correlation of EAS thickness and length measurements made on 3D EAUS and endoanal MRI along with a significant difference in grading of EAS atrophy between the two imaging methods. Limitations of current published studies include small study size and lack of gold standard comparison

indicating the need for further larger studies and evaluation of type of imaging modality with surgery and histology (Cazemier et al. 2006).

2.11 Currents methods of quantification of atrophy

One must emphasise that no universal criteria for the diagnosis of atrophy has as yet been established. In the studies mentioned so far interpretation of atrophy has been based on the subjective qualitative judgement of selected doctors. Endoanal MRI and external phased-array MRI only allow a semiquantitative assessment of fatty atrophy. Proton MRI spectroscopy has recently been used to quantify lipid content of muscle tissue non-invasively (Boesch et al. 1997; Schick et al. 1993; Szczepaniak et al. 1999; Kreis et al. 1996; Schick et al. 2002) and has been found to be comparable with that of biochemical measurements (Szczepaniak et al. 1999). Pfirrmann et al. 2004 were the first to evaluate the role of proton MR spectroscopy in the assessment of supraspinatus muscle fat content in asymptomatic volunteers and patients with supraspinatus tendon lesions. They concluded that proton MR spectroscopy was suitable in quantifying fatty atrophy of the supraspinatus muscle. This was followed by Chatoor et al. 2009 who looked at the role of MRI spectroscopy in the quantification of puborectalis muscle atrophy and correlated this with perineal dynamometry in asymptomatic controls and women with faecal incontinence. They reported a significant difference in the spectroscopic lipid content i.e. degree of atrophy between patients where muscle atrophy was subjectively scored as absent, moderate and severe. In addition, the patients with a mean apparent lipid content of more than 10% had significantly greater muscle fatigability as measured by perineal dynamometry compared with those subjects with less than 10% mean lipid content. The authors advocate MR spectroscopy as a promising objective measure of fatty atrophy of the puborectalis muscle secondary to obstetric muscular trauma, neurogenic injury and ageing.

One of the limitations of the use of MRI spectroscopy to quantify fatty atrophy of the external anal sphincter muscle is the size of the voxel which is positioned within the centre of the muscle using standard coronal and transverse T2 MRI sequences. The muscle within the area of the voxel undergoes MRI spectroscopy and subsequent quantification of fat and water, however the voxel can only be reduced to 5x5x5mm (normal size 10x10x10mm) and given the small size of the external anal sphincter

muscle, contamination within the voxel of laterally lying subcutaneous fat and medially lying longitudinal muscle can potentially occur.

To our knowledge, no study has as yet quantified fat replacement within the EAS which may be an important aspect of sphincter atrophy and outcome of surgical treatment. This thesis will be looking at other MRI techniques in addition to MR spectroscopy to quantify fatty atrophy of the EAS, correlating these findings with physiological measurements, symptom scores & other imaging modalities in assessing the role of atrophy and pelvic support structures in women with acute major obstetric tears and idiopathic faecal incontinence.

2.12 Summary

We know that symptoms of sphincter atrophy mirror symptoms of sphincter rupture. However, no gold standard has as yet been established for the detection and quantification of sphincter atrophy. In current clinical practice, a combination of methods in the form of electrophysiology, manometry, magnetic resonance imaging and endoanal ultrasonography are used to assess anal sphincter function and structure. This thesis will further explore the use of specific magnetic resonance imaging techniques in quantifying fatty atrophy of the anal sphincter musculature (chapter 5).

CHAPTER THREE

RISK FACTORS AND OUTCOMES OF THIRD AND FOURTH DEGREE ANAL SPHINCTER TEARS

3.1 Introduction

Vaginal delivery represents the single most important aetiological factor for anal sphincter injury and the subsequent development of faecal incontinence in women (Donnelly et al. 1998, Fynes et al. 1999). Three mechanisms of injury have been identified; direct anal sphincter muscle trauma, indirect traction pudendal neuropathy or a combination of these two (Snooks et al. 1990). Direct mechanical trauma may be overt i.e. identified clinically at the time of vaginal delivery or occult i.e. defect identified on endoanal ultrasound and not clinically at the time of delivery. Despite primary surgical repair the functional outcome of an overt injury is often disappointing with studies reporting a varied prevalence of faecal incontinence (range 7-58%) mainly due to persisting sphincter defects (Poen et al. 1998; Walsh et al. 1996; Sultan et al. 1994; Bek and Laurberg 1992; Haadem et al. 1988; Tetzschner et al. 1995; Mellerup Soresnsen et al. 1988; Nielsen et al. 1992). Regarding occult injury, Sultan et al. 1993 identified an occult sphincter injury in 35% of primiparous women on endoanal ultrasonography following vaginal delivery with one third of these women being symptomatic at 6 month follow up. Prevention of anal sphincter injuries is therefore paramount in order to prevent such sequelae. However, although we are aware of the risk factors associated with anal sphincter trauma the majority are not modifiable, only becoming apparent late in labour and therefore cannot be predicted or controlled for to prevent the occurrence of a third or fourth degree tear. In addition, many of the labour and delivery decisions are often dependent on complex inter-related risk factors.

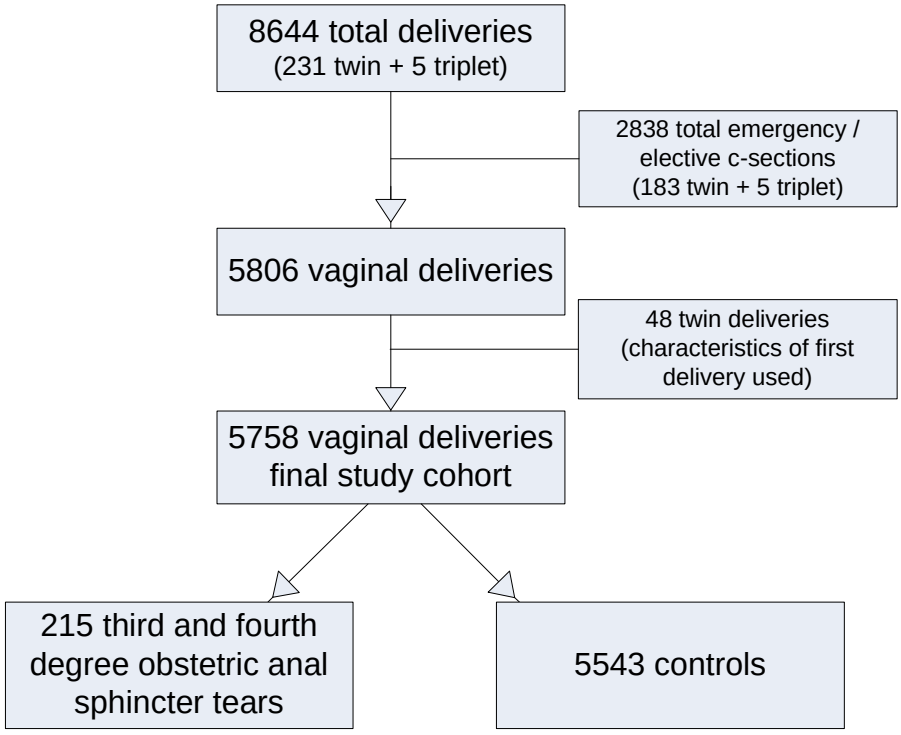
The primary objectives of our prospective study were three fold; firstly to define our study cohort selected from a large inner city tertiary teaching hospital; secondly to identify the obstetric, foetal and maternal risk factors associated with the development of third and fourth degree anal sphincter tears and their relationship to symptomatic outcome following primary sphincter repair; and thirdly to determine what value standard anorectal manometry and endoanal ultrasound are within this cohort with specific attention being paid to seeing whether symptom burden is correlated to any of these standard tests.

3.2 Methods

This prospective study was performed between 1st August 2009 and 31st January 2011 at University College Hospital, London, a tertiary referral unit with approximately 5000 deliveries per annum. The study was approved by The National Hospital for Neurology and Neurosurgery and Institute of Neurology Research Ethics Committee (10/H0716/10).

Information on all deliveries taking place at University College Hospital is entered by midwives, consultant and trainee obstetricians into a computerised maternity information system called eClipse. During the study period there were a total of 8644 deliveries including 231 twin deliveries and 5 triplet deliveries (figure 3.1). Delivery was by elective or emergency caesarean section in 2838 of these cases (including 183 twin deliveries and 5 triplet deliveries) and were excluded. Of the remaining 5806 vaginal deliveries, 48 were twin deliveries and in these cases the characteristics of the first foetus was used for analysis purposes thus making a final study population of 5758 cases.

Figure 3.1 – Total births at University College Hospital between August 09 and January 2011.



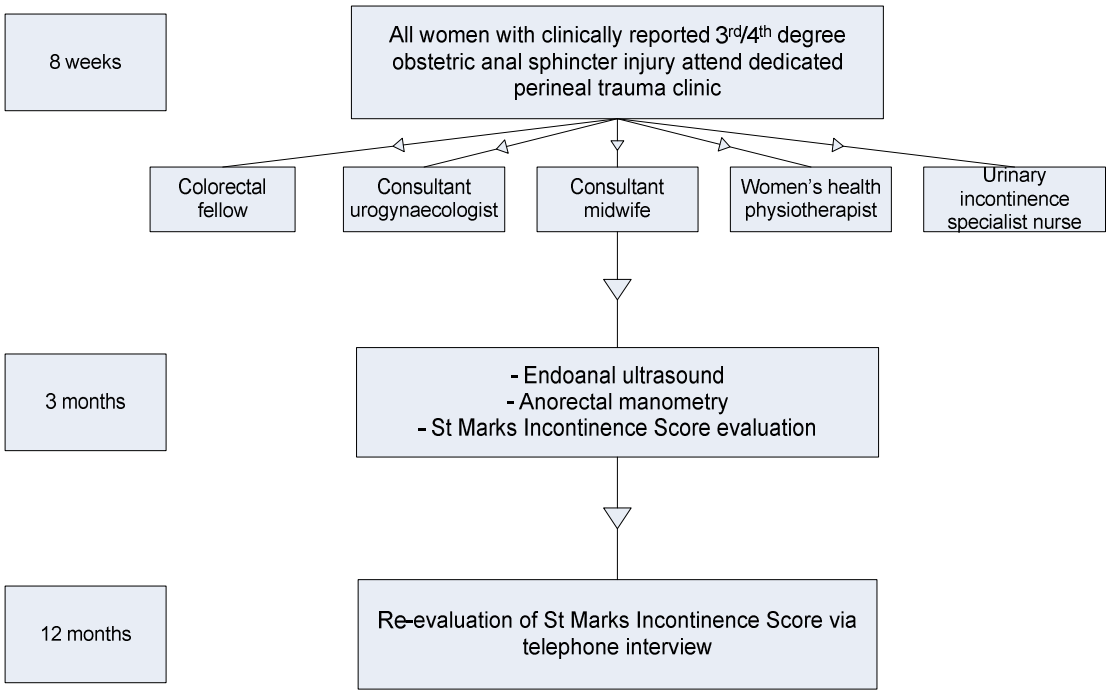
The primary outcome being sought in this cohort was the development of third or fourth degree anal sphincter tears which was diagnosed and classified using the Green Top Guideline Number 29 'Third and Fourth Degree Perineal Tears Management Guideline' accepted by the Royal College of Obstetricians and Gynaecologists (Fernando et al. 2007). In my data set the number of women with fourth degree tears was small and hence no distinction was made between third and fourth degree perineal tears in the analysis. A total of 215 women had third or fourth degree tears and the remaining 5543 women who had atraumatic deliveries constituted the control cohort. The obstetric variables such as maternal age, pre-pregnancy body mass index (BMI), duration of second stage of labour, use of epidural anaesthesia, instrumental delivery, episiotomy, parity and foetal characteristics such as foetal birthweight were then extracted from the database for each case and control. The data for foetal birthweight and second stage of labour were dichotomised at greater than 4kg and longer than one hour respectively as these cut offs have been identified in a number of studies as being associated with an

increased risk of obstetric anal sphincter tears (Cheng et al. 2004; Handa et al. 2001; Dupuis et al. 2004).

Exclusion criteria for my study were a history of anorectal surgery, subjects less than 18 years of age, medical comorbidities affecting bowel function and inflammatory bowel disease.

All women with third and fourth degree tears or symptoms of faecal incontinence were routinely referred to the birth injuries trauma clinic 8 weeks postpartum where they were initially reviewed by a consultant midwife and women's health physiotherapist with further review carried out by a urogynaecologist, colorectal research fellow or urinary incontinence specialist nurse if necessary. The patients then underwent anorectal assessment which was performed at 3 months postpartum with St Mark's Incontinence Score evaluation (short term SMIS), anorectal physiology and endoanal ultrasound (figure 3.2). Patients were subsequently contacted by telephone at 1 year postpartum. Verbal consent was obtained prior to commencing the telephone interview and clinical symptoms were then re-evaluated using the St Mark's Incontinence Score Questionnaire (medium term SMIS). Exclusion criteria for assessment of symptom load 12 months post delivery included women who were still breastfeeding, had a subsequent pregnancy or had anorectal surgery since their delivery. All women received the same post-operative care & pelvic floor rehabilitation. All women with persistent symptoms following primary repair and anorectal investigations were routinely referred for biofeedback therapy (Appendix 1).

Figure 3.2 – Flow chart demonstrating the management of patients with acute obstetric anal sphincter injury at UCLH.



3.2.1 Incontinence score questionnaire

The severity of faecal incontinence was graded with the validated St Mark's Incontinence Score (Vaizey et al. 1999) (see appendix 2) which takes into account consistency and frequency of anal incontinence (gas, liquid solid) and its effect on lifestyle, the need to wear a pad or plug, the use of constipating medication and the lack of ability to defer defecation for 15 minutes. The types of anal incontinence and its effect on lifestyle are scored from 0 (never) to 4 (daily), the need to wear pads and the use of medication 0 (no) or 2 (yes), and faecal urgency 0 (no) or 4 (yes) giving a total score of 0 (complete continence) to 24 (complete incontinence).

3.2.2 Anorectal manometry

Manometric assessment of the anal sphincter was performed with the patient positioned in the left lateral position using a balloon tipped water perfused catheter with 8 radially arranged ports lying 5 cm from the tip. The software program Medical Measurements System (MMS; http://www.mmsinternational.com/int/) was used for data acquisition.

The catheter was inserted into the rectum and the functional anal canal length was firstly defined by withdrawing the catheter until the high pressure zone of the anal canal was identified. A 1cm station pull through technique commencing at 6cm from the anal verge was then used to measure firstly the mean maximal resting pressure followed by the mean maximal squeeze pressure (i.e. the mean maximal increase above the resting pressure). The rectoanal inhibitory reflex (RAIR) was also recorded followed by the rectal sensitivity which involved inflation of the balloon at the tip of the catheter with air to determine the volume (in millilitres) required to create the sensation of threshold, urge and maximum tolerated volumes.

Anorectal mucosal electrosensitivity was measured using a bipolar electrode probe (Galtec) which was introduced into the anal canal and then the rectum. A constant current (electrical stimulation of 5 HZ and 10 HZ, along with a pulse width of 0.1msec and 0.5msec was applied in the anal canal and rectum respectively) was incrementally increased from 1 to 20 mA and 1 to 50 mA in the anus and rectum respectively until the patient indicated the threshold of sensation.

3.2.3 Endoanal Ultrasound

Endoanal ultrasonography was performed using the Hitachi automated system with a 10MHz rotating rectal probe and a water filled sonolucent hard plastic cone (diameter 17mm). The cone was covered with a condom and inserted into the anal canal with the patient in the left lateral/prone position. Serial digital images were recorded of the upper, middle and lower anal canal and stored in the radiology department's Picture Archiving and Communications System (PACS) database. The scans were performed by two radiologists who were both unaware of the anorectal manometry results and incontinence score. The integrity and quality of the external and internal anal sphincters were evaluated separately and recorded on the PACS reporting system.

For analysis purposes the endoanal ultrasound scoring system devised by Pinsk et al. 2009 (table 3.1) was used to score the anatomical and morphological appearances of the puborectalis, external and internal anal sphincters of each subject. The total score is calculated by adding points representing the integrity and quality of the anal sphincter muscles. A score of zero represents a normal endoanal ultrasound with no defects and normal muscle quality where as a score of 12 represents the poorest endoanal score with

loss of muscle integrity and changes in echogenicity i.e. atrophy in both internal and external anal sphincter muscles (Pinsk et al. 2009). Figures 3.3 and 3.4 demonstrate the endosonographic appearance of a defective and scarred anal sphincter.

Table 3.1 Pinsk et al. 2009 endoanal ultrasound scoring system for IAS and EAS defect and quality.

	Internal Anal Sphincter	**External Anal Sphincter**		
		Puborectalis	Mid-anal canal	Distal anal canal
Defect	0-2	0-2	0-2	0-2
Quality	0-1	0-1	0-1	0-1

Defect (absence of muscular fibres) at any level of IAS and/or EAS on USS image: 0 = no defect; 1 = segmental change in echogenicity (muscular fibres exist) = scar = partial defect; 2 = defect = gap with no muscle fibres.
Quality of IAS at mid-anal canal level and EAS at all three levels: 0 = normal echogenicity = normal quality; 1 = global (circumferential/patchy) change in echogenicity = atrophy.

Figure 3.3 Endoanal scan demonstrating a persistent anterior defect between 10 and 2 o'clock (between arrows) of the external (EAS) and internal (IAS) anal sphincter.

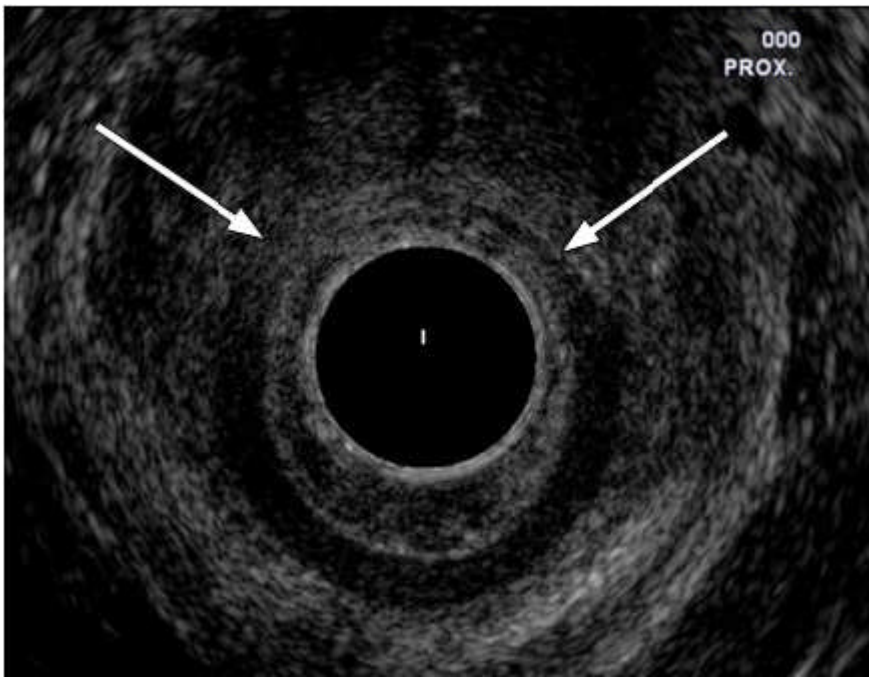
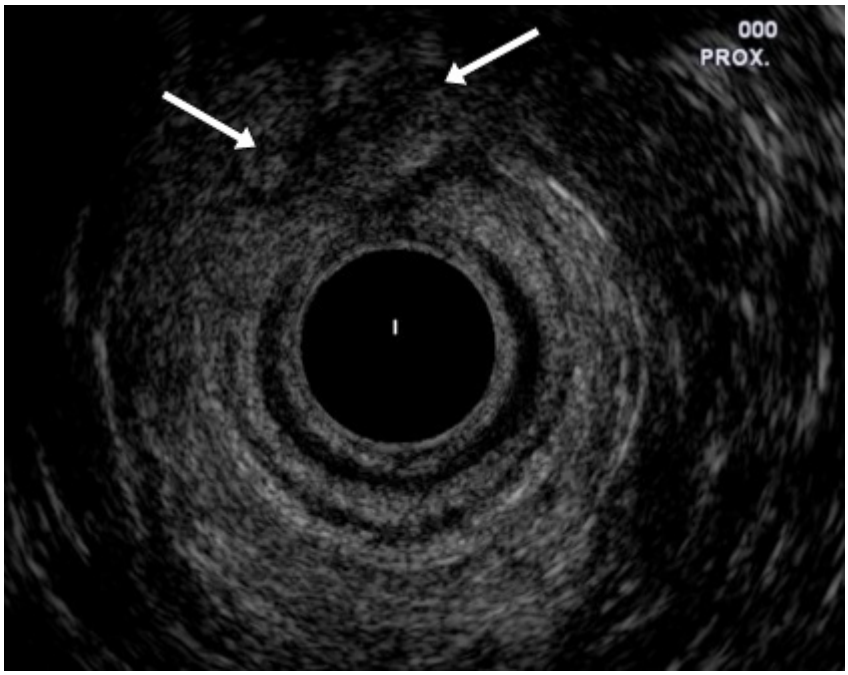


Figure 3.4 Endoanal scan demonstrating a primary overlap repair (between arrows) of the external (EAS) and internal (IAS) anal sphincter with residual scarring.



3.2.4 Data Analysis

Statistical analyses were performed using SPSS version 19 (SPSS Inc., Chicago, IL, USA). Continuous data was tested for normality using the Kolmogorov-Smirnov test. Summary statistics were reported as median and interquartile range or mean and standard deviation for continuous data and as frequencies for categorical data. Statistical significance of differences between the tear and non tear group for continuous variables was determined using the two sample t-test or Mann-Whitney U test where appropriate and for categorical variables using the Chi-squared test. For analysis purposes a foetal birthweight of greater than 4kg and/or a second stage of labour greater than 1 hour were defined as pathologic and hence the data was dichotomised at these limits.

Univariate logistic regression analysis was performed on each categorical maternal, foetal and obstetric risk factor using presence of third or fourth degree anal sphincter tear as the outcome variable. Those risk factors shown to be significantly associated with sphincter tears on univariate analysis were then entered into a multivariate logistic regression analysis to determine whether they were independently associated with anal sphincter tears. An adjusted odds ratio (OR) and 95% confidence interval (CI) were calculated for each risk factor.

Univariate logistic regression analysis was also used to determine the risk factors which were associated with anal incontinence.

Spearman's correlation coefficient with a two tailed test of significance was used to analyse non parametric data and the correlation between the endoanal ultrasound anal sphincter score, mean maximum resting and squeeze pressures and St Mark's Incontinence Score.

A P-value of less than 0.05 was considered to be statistically significant in all analyses.

3.3 Results

3.3.1 Maternal, obstetric and foetal risk factors

During the study period 5758 cases were reviewed, of these 215 (3.7%) sustained a third or fourth degree anal sphincter injury. Table 3.2 presents the maternal, obstetric

and foetal characteristics for women with third and fourth degree tears (study group) and those without third and fourth degree tears (control group).

Regarding mode of delivery, a greater proportion of women had a spontaneous vaginal delivery in the control group in comparison to the anal sphincter tear group (75% vs 49%). In addition, twice as many women had an instrument assisted vaginal delivery in the sphincter tear group compared to the control group. On further breakdown of instrumental deliveries, forceps were utilised in 28% of births in the sphincter tear group compared to 10% in the control group. Interestingly ventouse was less frequently used in the sphincter tear group than the control group (10% vs 12%). For the purposes of univariate & multivariate analyses, the categories of ‘forceps’, ‘ventouse’ and ‘both forceps and ventouse’ assisted deliveries were grouped as ‘instrumental deliveries’ due to the numbers within each subgroup being too small to allow meaningful analysis of their individual importance as risk factors for anal sphincter tears.

Table 3.2 Maternal, foetal and obstetric descriptive statistics for study group compared with control group.

Analysis by Mann Whitney U test (continuos data), Chi Squared test (categorical data)

Variable	Study group (3rd & 4th degree tears) (n=215)	Control group (no 3rd & 4th degree tears) (n=5543)	p values
Maternal age (yrs) median (IQR)	31 (27-35)	32 (28-35)	0.318
Nullip n(%)	186 (86.5%)	3325 (60%)	<0.001
Right or left mediolateral episiotomy n (%)	113 (52.6%)	1660 (29.9%)	<0.001
Mode of delivery n(%)			
SVD	106 (49.3%)	4154 (74.9%)	<0.001
Instrumental	109 (50.7%)	1389 (25.1%)	
Further breakdown of assisted vaginal delivery n(%)			
Forceps	61 (28.4%)	549 (9.9%)	<0.001
Ventouse	22 (10.2%)	676 (12.2%)	
Both forceps and ventouse	26 (12.1%)	164 (3%)	
Epidural n(%)	71 (33%)	1335 (24.1%)	0.003
BMI (kg/m^2) median (IQR)	23 (21-26)	23 (21-26)	0.511
Birthweight (g)			
>4000	28 (13%)	449 (8.1%)	0.01
<4000	187 (87%)	5094 (91.9%)	
Second stage (mins)			
>60	130 (60.5%)	2495 (45%)	<0.001
<60	85 (39.5%)	3048 (55%)	

Univariate analysis revealed several factors to be associated with a greater risk of third and fourth degree anal sphincter injury (table 3.3). Nulliparous mothers were at approximately 4 times greater risk of sustaining a sphincter tear compared to multiparous mothers. Babies greater than 4kg birthweight, mediolateral episiotomy, use of epidural, instrumental delivery and a second stage longer than 1 hour were all found to be significantly associated with anal sphincter injuries.

Table 3.3 Odds ratios derived from univariate regression analysis of categorical obstetric, maternal and foetal risk factors.

n= Number of cases with the risk factor and 3rd or 4th degree anal sphincter tear

N=Number of cases with the risk factor and no anal sphincter tear

OR= Odds ratio

CI= Confidence interval

SVD=Spontaneous vaginal delivery

Risk factor	Total	n/N	Rate of 3rd or 4th degree tears in women with and without the risk factor (%)	OR	95% CI	p value
Episiotomy						
Mediolateral episiotomy	1773	113/1660	6.4	2.59	1.97-3.4	<0.0001
No episiotomy	3985	102/3883	2.6			
Parity						
Nulliparous	3511	186/3325	5.3	4.28	2.88-6.36	<0.0001
Multiparous	2247	29/2218	1.3			
Epidural						
Epidural	1406	71/1335	5	1.55	1.16-2.08	0.003
No epidural	4352	144/4208	3.3			

Risk factor	Total	n/N	Rate of 3rd or 4th degree tears in women with and without the risk factor (%)	OR	95% CI	p value
Mode of delivery						
Instrumental	1498	109/1389	7.3	3.08	2.34-4.04	<0.0001
SVD	4260	106/4154	2.5			
Birthweight						
>4kg	477	28/449	5.9	1.64	1.08-2.48	0.02
<4kg	5281	187/5094	3.5			
Duration of second stage						
>60 mins	2625	130/2495	5	1.94	1.45-2.58	<0.0001
<60 mins	3133	85/3048	2.7			

All significant risk factors identified on univariate analysis were then entered into a multiple logistic regression analysis model to identify the risk factors that were independently associated with anal sphincter tears (table 3.4). Nulliparity, instrumental assisted delivery and foetal birth weight of greater than 4kg were all indicated to be significant independent risk factors for third and fourth degree tears. The use of episiotomy, epidural analgesia and a second stage of labour greater than 60 minutes were associated with a decreased risk of anal sphincter tear with an OR of 0.96 (CI 95% 0.63-1.58), 0.71 (CI 95% 0.49-1.04) and 0.95 (CI 95% 0.66-1.37) respectively although not statistically significant.

Although use of epidural, duration of second stage of labour and episiotomy were found to be associated with sphincter tears on univariate analysis they were failed to be found as independent risk factors.

Table 3.4 Multivariate regression analysis of all categorical and continuous risk factors.
OR= Odds ratio
CI= Confidence interval
SVD=Spontaneous vaginal delivery

Risk factor	OR	95% CI	p value
Episiotomy	0.96	0.63-1.58	0.998
Epidural	0.71	0.49-1.04	0.082
Parity	3.2	1.95-5.24	<0.0001
Mode of delivery (instrumental vs SVD)	3.13	1.93-5.06	<0.0001
Duration of second stage of labour	0.95	0.66-1.37	0.788
Foetal birthweight	2.05	1.29-3.28	0.003
Maternal age	N/A		0.796
Body mass index	N/A		0.994

3.3.2 Questionnaire

A total of 117 (54%) women attended follow up investigations and were assessed for anal sphincter structure and function and symptoms of faecal incontinence. The median time from delivery to follow up was 5 months (range 2-11 months). At follow up 51 women (44%) had faecal urgency and/or faecal incontinence. Of these 117 women, 11 were multiparous women of whom all were asymptomatic.

The mean and median St Mark's Incontinence Scores were 7 and 7 respectively (range 3-16). Incontinence to stool was present in 7 women (14%) and 35 women (69%) experienced flatus incontinence. Faecal urgency occurred in 35 women (69%). Of all these women 31 (61%) expressed some form of impact on daily living. No women used a pad or constipating agents to manage their incontinence symptoms.

No significant association was found between the presence of symptoms and the diagnosis of clinical tear (p=0.27 Chi squared 1.207).

Of these 117 women who were fully assessed at initial follow up, 70 were contacted via telephone between 12 and 18 months (median 12 months) to reassess their medium term symptoms using the St Mark's Incontinence Questionnaire. Of the 70 women, 29 (41%) had symptoms of incontinence at initial follow up and 15 of these (52%) remained symptomatic at medium term follow up (figure 3.5). The incontinence score decreased between initial and medium term follow up (mean 8 +/- 4 vs 5 +/- 3, p=0.01). None of the asymptomatic women at initial follow up reported any deterioration of bowel function.

Figure 3.5 – Flow chart summarising women with clinically identified anal sphincter tears and symptoms at initial and medium term follow up.

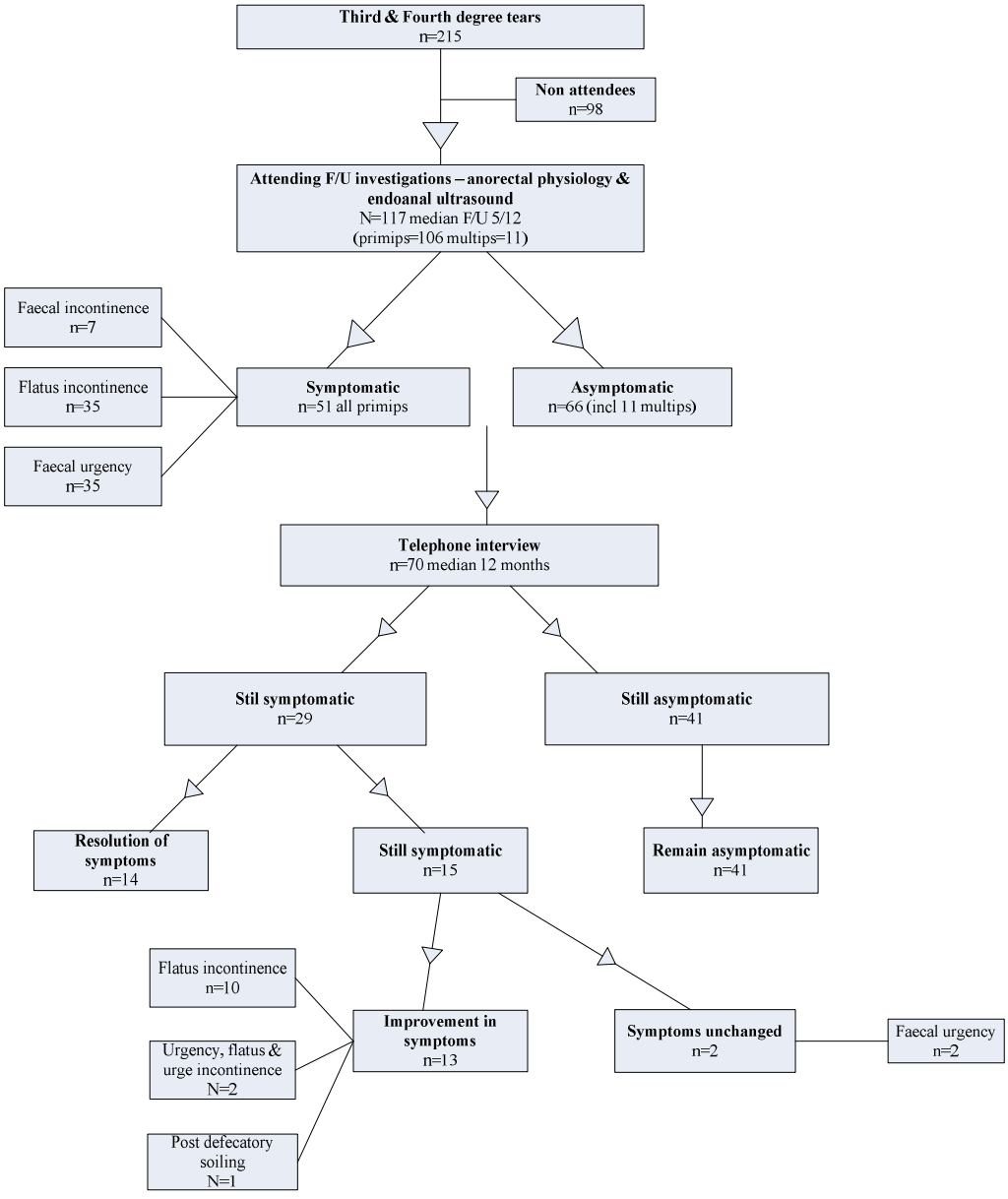


Table 3.5 shows the association of faecal incontinence and different variables amongst the obstetric anal sphincter tear group on univariate analysis, using continent women as the reference group (St Marks Incontinence Score =0). Maternal age appeared to be the only risk factor to be significantly associated with the development of faecal incontinence (OR 1.1 95% CI 0.94-1.9). Multivariate analysis was not performed due to small sample size and due to the identification of a single risk factor associated with the development of symptoms on univariate analysis.

Table 3.5 Univariate regression analysis for risk factors for faecal incontinence in women with 3rd and 4th obstetric anal sphincter injuries.
OR= Odds ratio
CI= Confidence interval
SVD=Spontaneous vaginal delivery

Risk factor	OR	95% CI	p value
Foetal birthweight	0.84	0.28-2.55	0.764
Maternal age	1.1	0.94-1.9	0.006
Body Mass Index	1.02	0.92-1.13	0.725
Duration of second stage	0.79	0.37-1.70	0.543
Episiotomy	1.71	0.82-3.59	0.153
Mode of delivery (instrumental v SVD)	1.55	0.75-3.24	0.24
Parity	2.21	0.56-8.78	0.26
Epidural	1.03	0.46-2.30	0.94

3.3.3 Anorectal Manometry

Of the 117 women that underwent anorectal manometry, 66 were asymptomatic and 51 had complaints of faecal urgency and anal incontinence.

Table 3.6 shows the data for anorectal manometry and anal and rectal sensitivity measurements. Both the mean resting and mean squeeze pressures were lower in the group of symptomatic women than the asymptomatic group (table 3.6 and figure 3.6 and 3.7). In addition, the asymptomatic group had lower anal and rectal sensitivity and rectal capacity in comparison to the symptomatic group (table 3.6 and figure 3.8, 3.9

and 3.10). However no significant association between these groups was found with regards to mean resting and squeeze pressures or anal and rectal sensitivity.

Table 3.6 Anorectal manometry, rectal sensitivity, anal and rectal sensation.
Values are mean (SD)
MRP mean maximum resting pressure, MSP mean maximum squeeze pressure increment, TV threshold volume, UV urge volume, MTV maximum tolerated volume

	All n=117	**Faecal urgency & incontinence n= 51**	**Continent n=66**	**P value**
Anorectal manometry (cm H20)				
MRP	79 (26)	75 (26)	83 (25)	0.14
MSP	66 (35)	62 (34)	69 (35)	0.29
Rectal sensitivity (ml)				
TV	39 (19)	41 (35)	40 (18)	0.82
UV	86 (28)	90 (40)	85 (23)	0.42
MTV	159 (52)	163 (59)	162 (55)	0.94
Anal sensation (mA)	8.1 (2.8)	8.3 (2.8)	7.9 (2.8)	0.46
Rectal sensation (mA)	22.8 (8.4)	22.3 (7.6)	23 (9.5)	0.46

Figure 3.6 Mean maximum resting pressure in 117 women with third or fourth degree tears subdivided into incontinent (n=51) and continent (n=66) groups.

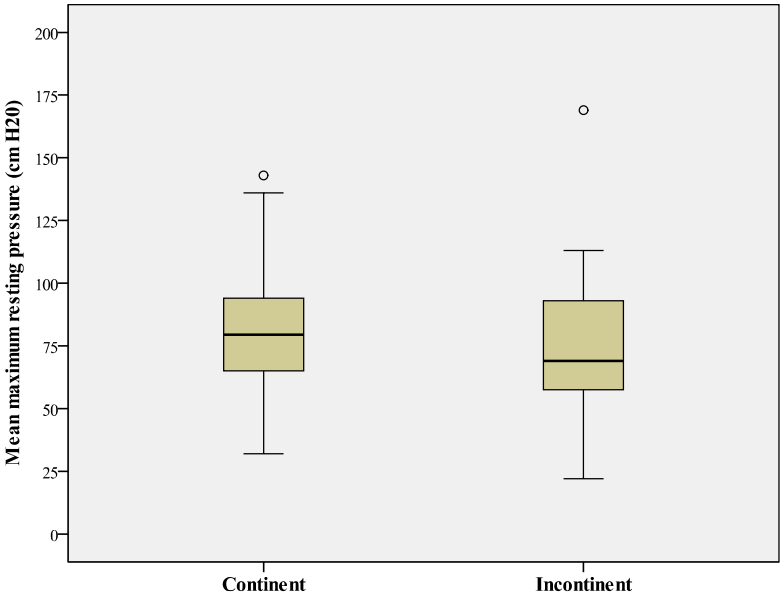


Figure 3.7 Mean maximum squeeze pressure increment in 117 women with third or fourth degree tears subdivided into incontinent (n=51) and continent (n=66) groups.

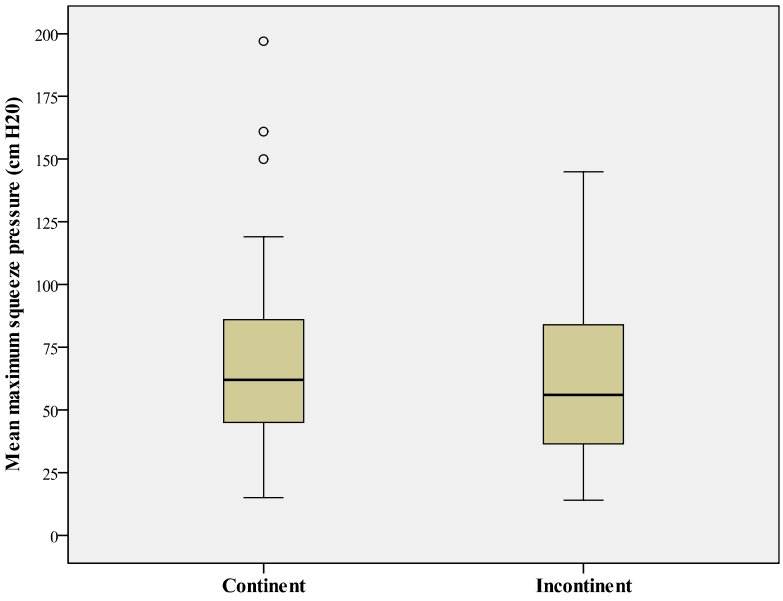


Figure 3.8 Anal sensation in 117 women with third or fourth degree tears subdivided into incontinent (n=51) and continent (n=66) groups.

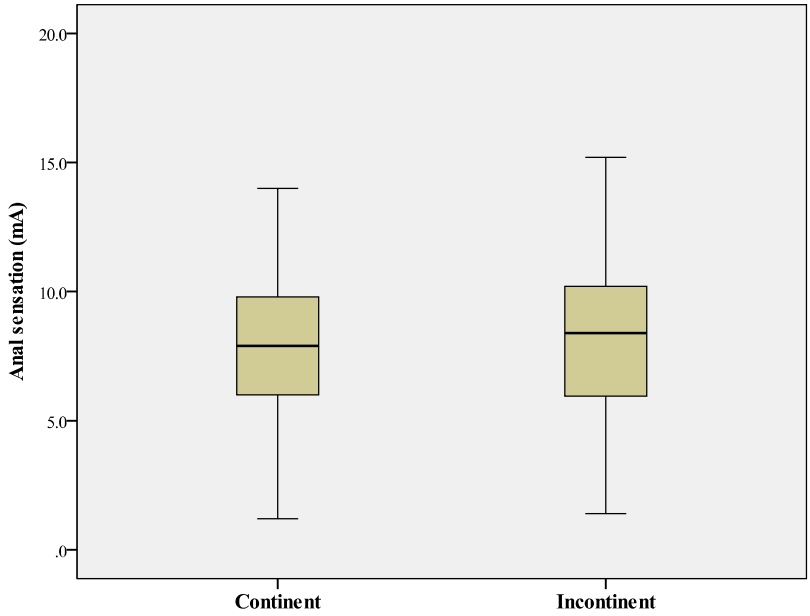


Figure 3.9 Rectal sensation in 117 women with third or fourth degree tears subdivided into incontinent (n=51) and continent (n=66) groups.

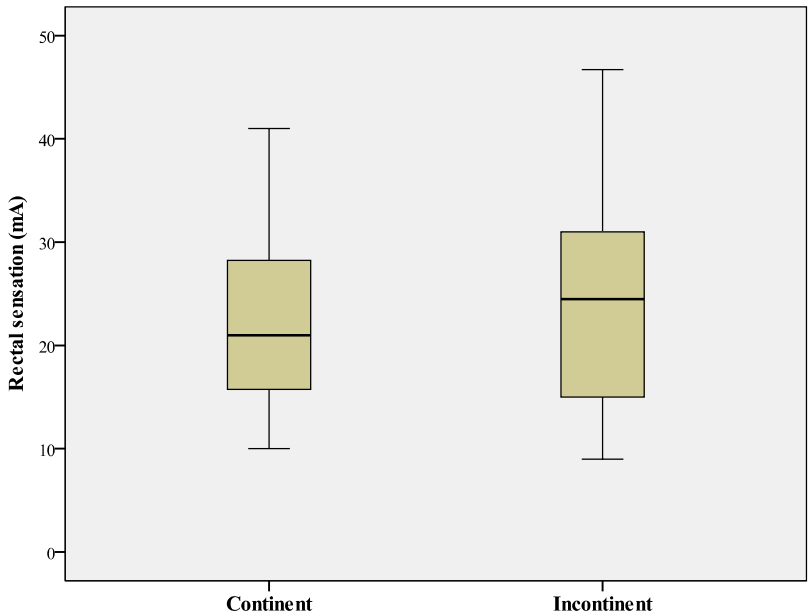


Figure 3.10 Rectal sensitivity in 117 women with third or fourth degree tears subdivided into incontinent (n=51) and continent (n=66) groups.

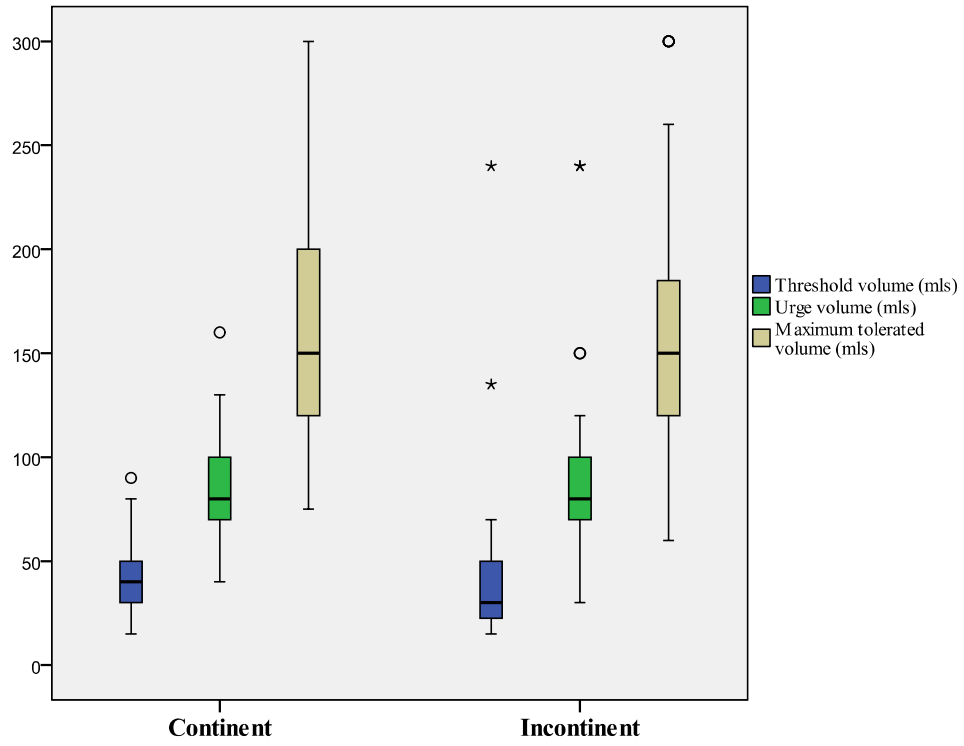


Table 3.7 represents the percentage of asymptomatic and symptomatic women with mean resting and mean squeeze pressures and anal and rectal sensitivity measurements outside of the normal range used in our unit. A greater number of symptomatic women had abnormal mean resting and mean squeeze pressures in comparison to the asymptomatic women. In addition, more asymptomatic women had an abnormal anal sensitivity in comparison to the symptomatic women.

Table 3.7 Percentage of incontinent and continent women with anorectal manometry parameters outside the normal range. The number of women is represented in the parentheses.

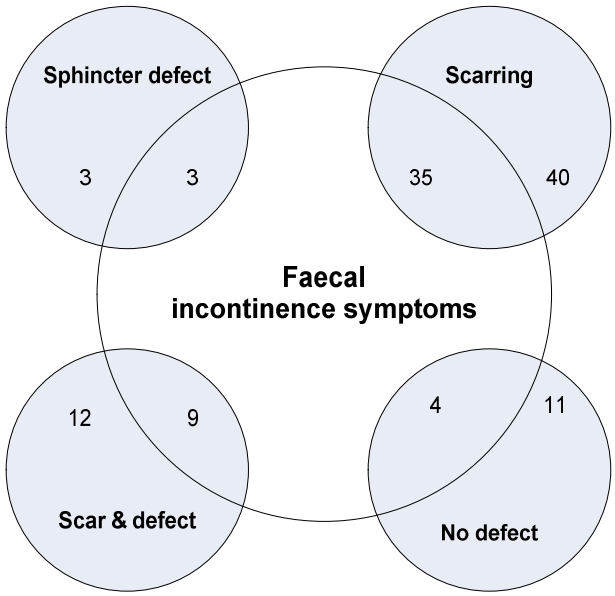
	Faecal urgency & incontinence n= 51	Continent n=66	P value
Anorectal manometry			
MRP	28% (14)	11% (7)	0.03
MSP	47% (24)	32% (21)	0.14
Rectal sensitivity			
TV	8% (4)	8% (5)	0.96
UV	10% (5)	3% (2)	0.25
MTV	16% (8)	11% (7)	0.59
Anal sensation	33% (17)	32% (21)	0.86
Rectal sensation	9.8% (5)	3% (2)	0.25

3.3.4 Endoanal ultrasonography

With endosonography, defects in one or both sphincters were reported in 6 women (5%). Scarring was reported in 75 women (64%) and scarring and defect was repoprted in 21 women (18%). No defect or scarring was reported in 15 women (13%). Incontinence was reported by 3 of 6 women with isolated or combined sphincter or puborectalis defects, 35 (47%) of 75 women with scarring of one or both sphincters and puborectalis and 9 (43%) of 21 women with combined scarring and defect to one or both sphincters and puborectalis (figure 3.11). Not having a sphincter defect or scarring did not imply absence of anal incontinence: four out of 15 (27%) women with intact non scarred sphincters reported symptoms of anal incontinence.

Again no significant association between symptoms of faecal incontinence and sonographically detected anal sphincter defects or scarring was detected (p=0.26 Chi squared=1.292).

Figure 3.11 Venn diagram demonstrating the relationship between EAUS findings and symptoms.



3.3.5 Internal anal sphincter correlations

Neither mean maximum resting pressure or symptoms were found to significantly correlate with individual internal anal sphincter defect score, quality score or combined defect and quality score.

Table 3.8 Correlation between IAS endoanals ultrasound score and mean maximum resting pressure and St Mark's Incontinence score.

	Mean maximum resting pressure	SMIS
IAS defect		
Spearman's rho	-0.127	0.074
p value (two tailed)	0.179	0.433
IAS quality		
Spearman's rho	-0.048	-0.039
p value (two tailed)	0.614	0.679
IAS total score		
Spearman's rho	-0.138	0.062
p value (two tailed)	0.142	0.511

3.3.6 External anal sphincter correlations

A significant negative correlation was found between total score of external anal sphincter and mean maximum squeeze pressure (-0.249, P=0.008) (table 3.9). No similar trend was found between total external anal sphincter score and incontinence score or individual mid and distal external anal sphincter defect and quality scores and mean maximum squeeze pressure and incontinence score.

Table 3.9 Correlation between EAS endoanal ultrasound score and mean maximum squeeze pressure and incontinence score. *P<0.05 significance level

	Mean maximum squeeze pressure		SMIS	
	Spearman's rho	**p value (2 tailed)**	**Spearman's rho**	**p value (2 tailed)**
Mid EAS				
Defect	-0.191	0.065	0.183	0.077
Quality	NA	NA	NA	NA
Distal EAS				
Defect	-0.149	0.152	-0.038	0.716
Quality	NA	NA	-0.085	0.415
Total EAS score	-0.249	0.008*	0.072	0.449

3.3.7 Combined sphincter correlations

There was a statistically significant correlation between squeeze pressure and total endoanal ultrasound score (-0.413, P=0.001) (table 3.10). No correlation was found between resting pressure or incontinence score with total endoanal ultrasound score.

Table 3.10 Correlation between resting pressure, squeeze pressure, incontinence score and total endoanal ultrasound score. *P<0.05 significance level

	Endoanal USS total score	
	Spearman's rho	**p value (2 tailed)**
Rest pressure	-0.196	0.058
Squeeze pressure	-0.413	0.001*
SMIS	0.104	0.316

3.4 Discussion

The goal of this prospective population based study was firstly to identify the obstetric, foetal and maternal risk factors associated with third and fourth degree anal sphincter tears and relation of these risk factors to changes in symptom load and secondly to see if there was an association between symptoms, anorectal function quantified by physiology and structure assessed by anal endosonography in a cohort selected from a large inner city tertiary teaching hospital.

The incidence of third and fourth degree tears during vaginal delivery regardless of parity in my study population was 3.7% (215/5758) which is comparable to and slightly higher to some European studies (Hudelist et al. 2005; Sultan et al. 1994; Gupta et al. 2003; Samuelsson et al. 2000) but far below the incidence reported by studies from the United States (Richter et al. 2002; Goldberg et al. 2003; Robinson et al. 1999; Handa et al. 2001; Green and Soohoo 1989; Peleg et al. 1999). This discrepancy may be attributable to the variation amongst study populations and number of institutions involved in the study along with differing practices and policies regarding the type of episiotomies performed, the method used in the diagnosis of third and fourth degree sphincter tears, the expertise of the medical staff managing the delivery and the decision to use vacuum and/or forceps.

3.4.1 Risk factors associated with anal sphincter tears

In my study cohort nulliparity, babies greater than 4kg birthweight, mediolateral episiotomy, use of epidural, instrumental delivery and a second stage longer than 1 hour were all found to be significantly associated with anal sphincter injuries. Obstetric

interventions in particular instrumental assisted delivery is a well known cause of third and fourth degree sphincter tears with a number of retrospective studies reporting unequivocal agreement that forceps assisted vaginal delivery is an independent risk factor for anal sphincter tears (Baumann et al. 2007; de Leeuw et al. 2001; Poen et al. 1997; Combs et al. 1990; Riskin-Mashiah et al. 2002; Angioil et al. 2000; Christianson et al. 2003; Richter et al. 2002). In theory forceps cause more damage than ventouse extractors as the blade occupies a larger area of the pelvic outlet exerting greater pressure on the perineum during traction (Sultan et al. 1993). In my study group there was a lower frequency of tears in the ventouse assisted delivery group. Vacuum assisted delivery has been shown to be associated with a significantly lower risk of anal sphincter trauma compared to forceps assisted delivery and has subsequently been adopted as the instrument of first choice by the Royal College of Obstetricians and Gynaecologists (Johanson and Menon 2000; de Leeuw et al. 2001; Combs et al. 1990; Sultan et al. 1994; Poen et al. 1997; Williams 2003; Baumann et al. 2007; Andrews et al. 2006; Dandolu et al. 2005; Crawford et al. 1993). Our results support this observation with 61 (10%) of 610 forceps deliveries and 22 (3.2%) of 698 vacuum deliveries resulting in anal sphincter tears. In contrast to my findings, some studies have shown anal sphincter tears to complicate 60% of forceps deliveries (Eogan et al. 2006) with others reporting incidences as low as 1.6 % and 4.2% (Hudelist et al. 2005; Gupta et al. 2003). One possible explanation of this variation in forceps related anal sphincter tears may be due to the level of experience of the obstetrician carrying out the delivery. My study cohort was derived from a busy obstetric unit in an inner city teaching hospital and therefore the high turnover of trainees may have accounted for the higher rate of forceps associated anal sphincter tears in comparison to some other institutions.

Univariate analysis demonstrated nulliparity, high foetal birthweight, mediolateral episiotomy, epidural use, instrumental delivery and second stage of longer than 60 minutes duration to be associated with a greater risk of anal sphincter tears which remains in keeping with previous studies (Gerdin et al. 2007; Sultan et al. 1994; de Leeuw et al. 2001; Angiolo et al. 2000; Varma et al. 1999; Williams et al. 2005; Samuelsson et al. 2000; Zetterstrom et al. 1999; Bek and Laurberg 1992; Helwig et al. 1993; Berard et al. 1998; Combs et al. 1990; Sultan et al. 1993; Robinson et al. 1999; Eason et al. 2000; Samuellson et al. 2000; Sultan et al. 1994; Bek et al. 1992; Poen et al. 1997; Buekens et al. 1985). In my study, nulliparity was the most prominent factor in

the strength of association with anal sphincter tears (OR 4.3, 95% CI 2.9-6.4) (Baumann et al. 2007). One possible explanation for this observation is the difference in strength and laxity of the connective tissue between the nulliparas and multiparas.

Multivariate analysis found the non modifiable variables nulliparity and foetal birthweight greater than 4kg and the modifiable variable instrumental assisted delivery as independent risk factors in the development of anal sphincter tears which is in accordance with previous studies (Hudelist et al. 2004; Williams 2003; Sultan et al. 1994; de Leeuw et al. 2001; Varma et al. 1999; Angioli et al. 2000; Williams et al. 2005; Samuelsson et al. 2000; Zetterstrom et al. 1999; Helwig et al. 1993; Berard et al. 1998; Combs et al. 1990; Sultan et al. 1993; Robinson et al. 1999; Eason et al. 2000). One presumes that a larger baby would invoke greater mechanical stresses upon the perineum during delivery rendering it more susceptible to disruption. Although episiotomy, use of epidural and longer duration of second stage of labour were found to be significant risk factors in the univariate analysis their strong interconnection accounts for why they failed to be shown as independent risk factors on multivariate analysis.

The use of episiotomy to protect against anal sphincter tears remains a subject of constant debate. In my study, mediolateral episiotomy alone was found to be protective to the perineum (OR 0.96 95% CI 0.63-1.58) which is consistent with studies by Handa et al. 2001 and Dandolou et al. 2005 who both reported a 10% reduction in the incidence of sphincter tears with the use of an episiotomy. By contrast Bek and Laurberg 1992, Williams et al. 2003 and Walsh et al. 1996 demonstrated an increased risk of anal sphincter injury with mediolateral episiotomy whilst Jander and Lyrenas 2001 and Bodner-Adler et al. 2001 found no association between the two. One must be cautious when drawing conclusions from these studies due to small study numbers, lack of analysis of confounding variables by multiple regression techniques and no use of endoanal ultrasonography to confirm the true incidence of a third or fourth degree tear. Ideally a randomised prospective trial looking at the association of episiotomy to anal sphincter trauma is required.

Epidural analgesia has been consistently associated with increased duration of second stage of labour, instrumental assisted vaginal delivery and episiotomies (Gerdin et al. 2007; Robinson et al. 1999; Howell et al. 2001). My univariate analysis seemed to

confirm this, however when controlling for these risk factors I found epidural analgesia to have a protective effect on the anal sphincter. This observation remains in keeping with Baumann et al. 2007, Eskander et al. 2009 and Samuellson et al. 2000 and differs from Poen et al. 1997, Gerdin et al. 2007 and Sultan et al. 1994 all of whom reported an increased risk of anal sphincter disruption with epidural use. In particular Poen et al. 1997 demonstrated a greater number of sphincter tears in nulliparous women having epidurals. It is possible that women with epidurals are tearing more extensively due to loss of sensation which normally acts as a precursor of perineal overstretching.

On multivariate analysis no association between prolonged second stage and incidence of anal sphincter injury was found. I used a cut off period of 60 minutes or greater when defining length of second stage based on a number of studies (Cheng et al. 2004; Handa et al. 2001; Dupuis et al. 2004) having reported an association with anal sphincter tears. However Cheng et al. 2004 found one third of nulliparous women who had a second stage of longer than 4 hours sustained a third or fourth degree tear and remained a significant risk factor after controlling for other risk factors (OR 1.33). Could it possibly be that the risk of sphincter trauma may be associated with a longer duration of the second stage of labour?

In terms of limitations, my study population was composed from a single institution requiring validation with multiple centres, variation in documentation, coding practices and data collection were minimal. Other limitations were that no details regarding antepartum bowel symptoms were entered and only obstetric details on current births and not earlier deliveries were entered into the computerised database. Due to the observational nature of the study, I was limited to the information entered on the database and therefore other potential confounding variables such as maternal ethnicity, birth delivery position and level of experience and training of obstetricians performing episiotomies and instrumental deliveries which were not documented onto the database could not be included in our analysis.

3.4.2 Symptoms and anorectal structure and function

In my study all 51 of the 117 women attending for initial follow up investigations (median 5 months) were symptomatic primiparous women. No significant association between the presence of symptoms and diagnosis of clinical tear was found in my study

cohort. All third and fourth degree sphincter tears were grouped together in my analysis due to small study numbers therefore not allowing myself to distinguish if bowel symptoms were more prominent following a greater degree of sphincter trauma. In addition, I did not differentiate between 3a, 3b and 3c tears due to the subjective nature of this diagnosis so it may be that women with partial third degree tears have a better prognosis than those with a complete third degree tear.

At 12 month follow up 51% (15 of 29) of women still had symptoms of faecal incontinence although the majority of these women (13 of 15) reported an improvement in symptoms. This improvement may be explained by the resolution of impaired pudendal nerve function following delivery and the cessation of breastfeeding which restores oestrogen levels and reactivates pelvic floor oestrogen receptors resulting in improved continence (Zetterstrom et al. 1999). The prevalence of faecal incontinence post primary sphincter repair varies between 7 to 58% in previous studies (Poen et al. 1998; Walsh et al. 1996; Sultan et al. 1994; Bek and Laurberg 1992; Haadem et al. 1988; Tetzschner et al. 1995; Mellerup et al. 1988; Nielsen et al. 1992). This variation in frequencies may be secondary to the lack of consistency in the symptom score questionnaires used, the variation in the definition of severity of symptoms and the under reporting of symptoms by women who are too embarrassed to ask for help. In our study the symptom score used scored faecal urgency, flatus incontinence and the need to wear a pad or use constipating agents as separate points all contributing to the final incontinence score. This poor outcome may be due to inadequate repair or insufficient healing of the primary repair resulting in a persistent sphincter defect or non identified multiple sphincter defects with the repair of only one of these defects (Laine et al. 2011).

Endoanal ultrasonography demonstrated persistent defects in 23% (27 of 117) of women with primarily repaired third or fourth degree sphincter tears. Of these, 3 of the 6 women (50%) which had a persistent defect were symptomatic and 9 of the 21 women (43%) with scarring in combination with a persistent defect remained symptomatic. Once again no significant association between symptoms of faecal incontinence and sonographically detected anal sphincter defects or scarring was found. Sultan et al. 1994 identified a persistent defect in up to 85% of women who had undergone a primary sphincter repair with endoanal ultrasound performed at 3 months postpartum which is

greater in frequency to that found in this study. Interestingly, 4 of 15 (27%) women who had intact non scarred sphincters on endoanal ultrasound reported symptoms of incontinence implicating other causes beyond the sphincter such as pelvic floor neuropathy or other structural pelvic muscle disruption. Fifty five patients (55/102 54%) with evidence of a sphincter defect and or scarring on endoanal ultrasound reported no symptoms at initial follow up which can be attributed to their youth and the compensatory role that the puborectalis muscle may play in the maintenance of faecal continence. One can postulate that some of these women may have deterioration in their continence as they have further vaginal deliveries, get older and go through the menopause.

Although this study showed an improvement in faecal incontinence symptoms over time the follow up period is short and hence in order to determine the influence of obstetric anal sphincter trauma on continence further long term follow up is required. My study did not have a comparative control group of women without anal sphincter trauma who underwent the same anorectal follow up investigations and I was therefore unable to assess the incidence of incontinence symptoms in women with intact anal sphincters or identify women with occult tears. In addition, the 54% attendance rate for follow up investigations could have potentially biased my results as mainly symptomatic women may have attended their appointments resulting in a possible over estimation of incontinence scores and abnormalities in anorectal function in this group.

Using the proposed scoring system devised by Pinsk et al. 2009 which takes into account both defects and changes in quality of the internal and external anal sphincters as seen on endoanal ultrasound, I found a significant negative correlation firstly between the total endoanal ultrasound score for the EAS and mean maximum squeeze pressure ($r=-0.249$, $p=0.008$) and secondly between total endoanal ultrasound score and mean maximum squeeze pressure ($r=-0.413$, $p=0.001$). No correlations were found between symptom score and IAS, EAS or total endoanal ultrasound score once again pointing to a possible neuromuscular component. To my knowledge, the Pinsk score (Pinsk et al. 2009) has been the only proposed score to incorporate changes in quality of the muscle i.e. thinning or atrophy visualised on endoanal ultrasound. Anal endosonography is the conventional imaging modality used to define the anatomy and depict structural defects of the anal sphincter complex with endoanal or endocoil MRI

being proved to be an excellent tool for the detection of anal sphincter atrophy (West et al. 2005). Further studies comparing the accuracy of this ultrasound scoring system with endocoil MRI are required and therefore conclusions drawn from this data must be taken with caution.

In this study, although the mean resting and squeeze pressures along with anal sensation and rectal capacity were lower in the symptomatic women compared to the asymptomatic women with clinically diagnosed anal sphincter tears, no significant difference between the two groups was established. This could be accounted for by neurological injury to the pudendal nerve rather than traumatic injury to the sphincter. Snooks et al. has contributed a large body of work demonstrating the influence of pudendal nerve injury to the development of faecal incontinence following vaginal delivery (Snooks et al. 1990, Snooks et al. 1984; Snooks et al. 1985). Of 20 women with an obstetric external anal sphincter tear and subsequent faecal incontinence 60% were reported to have evidence of co-existing pudendal nerve damage (Snooks et al. 1985). In 1984, they reported a prolonged PNTML in a significant number of primiparous and multiparous women 48-72 hours after vaginal delivery compared to non pregnant healthy multiparous women and that at 2 months post partum, recovery in nerve function was least complete in the multiparous women delivered by forceps (Snooks et al. 1984). They also suggested parity as an important contributing factor to the development of pelvic floor dysfunction (Snooks et al. 1984; Snooks et al. 1986). Conflicting reports have since shown normal pudendal nerve function in symptomatic women with persisting sphincter defects following primary repair indicating mechanical sphincter trauma as the primary cause of faecal incontinence symptoms (Poen et al. 1998; Sultan et al. 1994). The clinical relevance of measuring PNTML has recently become a controversial topic amongst physicians due to studies reporting poor correlation with anorectal manometry (Thomas et al. 2002; Tetzschner et al. 1995; Hill et al. 1994; Vaccaro et al. 1995; Osterberg et al. 2000; Rasmussen et al. 2000; Sulleabhain et al. 2001) and symptoms (Vaizey et al. 1999; Ricciardi et al. 2006) as well as inadequate sensitivity and specificity. Based on this evidence and the lack of availability of an accurate physiological test I did not quantify pudendal nerve function in my cohort and therefore I was unable to comment on the neurological contribution to changes in function and symptoms between the two groups.

3.4.3 Risk factors associated with faecal incontinence

There is a vast variation in the results of studies examining the obstetric factors associated with symptoms of faecal incontinence in patients with obstetric anal sphincter injury. I have identified increasing maternal age as a risk factor of faecal incontinence following an obstetric anal sphincter tear which is in agreement with other studies (Pollack et al. 2004; Zetterstrom et al. 1999). The odds ratio in my results indicate that a thirty year old woman with a third or fourth degree anal sphincter tear is at double the risk of developing faecal incontinence in comparison to a twenty year old lady with a tear. This finding is highly relevant considering the observation that the average age of primparous mothers is on the rise. Possible explanations of this association may be due to sarcopenia, the degenerative loss of mass and strength of skeletal muscle associated with aging or changes in structure and function of connective tissue with advanced age (Zetterstrom et al. 1999). I was unable to identify an association between other foetal, maternal and obstetric variables such as foetal birthweight, duration of second stage, BMI, use of episiotomy or epidural, instrumental delivery and parity and faecal incontinence. Again I did not include a group of matched controls without anal sphincter tear and therefore was unable to determine the influence of anal sphincter tears with symptoms.

CHAPTER FOUR

VAGINAL MANOMETRY IN THE ASSESSMENT OF PELVIC FLOOR STRENGTH

4.1 Introduction

The pelvic floor is a complex structure comprising the pelvic diaphragm (pubococcygeus, puborectalis and ileococcygeus muscles forming the levator ani), urogenital diaphragm (ischiocavernosus, bulbospongiosus and superficial transverse perineii muscles) and perineal body. The pelvic floor muscles play an imperative role in providing pelvic organ support and maintaining urinary and faecal continence through elevation and occlusion of the pelvic openings upon contraction (Retzky and Rogers 1995; Frawley et al. 2006). More specifically, voluntary contraction of the puborectalis component of the levator ani has been reported to enhance the faecal continence mechanism firstly by contributing to the proximal anal squeeze pressure (Liu et al. 2006) and secondly by decreasing the anorectal angle. Based on these observations it can be postulated that faecal continence may be preserved by the puborectalis muscle (PRM) in cases of obstetric anal sphincter trauma.

Due to the absence of a vaginal intrinsic sphincter mechanism it is thought that vaginal pressure can act as a measure of the strength of the pelvic floor musculature. Investigators have attempted to use various devices such as the perineometer, balloons and vaginal cones to measure the vaginal pressure as a marker of pelvic floor muscle strength (Kegel 1948; Hahn 1996; Bo 1992; Shafik 1997) however none of these techniques measure absolute pressure. As yet there is no gold standard tool to quantify PRM strength. Recent work carried out by Guaderrama et al. 2005 has been the first to identify a vaginal high pressure zone with the use of the pull through technique with a four channel water perfused vaginal manometry catheter in 14 healthy nulliparous women. The authors concluded the high pressure zone to be reflective of pelvic floor contraction and described it be 3-4cm in length and located in the distal part of the vagina approximately 2cm above the hymen.

As yet to my knowledge no studies have used vaginal manometry to identify changes to the vaginal high pressure zone in symptomatic patients. The objective of this study was firstly to determine the vaginal pressure profile (during rest and voluntary contraction) in symptomatic women with acute obstetric anal sphincter injuries, and secondly to compare squeeze pressures measured by vaginal manometry and anorectal manometry.

4.2 Methods

4.2.1 Participants

This prospective study was performed between January 2010 and January 2011 at University College Hospital, London. The study group consisted of 44 consecutive primiparous women (mean age 32 years range 18-42 years) with clinically diagnosed third or fourth degree anal sphincter tears referred from the birth injuries clinic to the gastrointestinal physiology unit for routine follow up assessment of anorectal function. The control group consisted of 14 healthy nulliparous women (mean age 33 years range 25-40 years) who were recruited by advertisement via webmail to employees working within the trust and students enrolled at the affiliated University College London. All participants underwent full clinical history assessment using the St Mark's Incontinence questionnaire (Vaizey et al. 1999) along with vaginal and anorectal manometry.

The study was approved by The National Hospital for Neurology and Neurosurgery and Institute of Neurology Research Ethics Committee (10/H0716/10) and written consent was obtained from all participating subjects.

Exclusion criteria for both controls and study subjects were a history of anorectal surgery (with exception to primary anal sphincter repair in the study group), subjects less than 18 years of age, medical co morbidities affecting bowel function i.e. diabetes, endocrine disease, scleroderma, and inflammatory bowel disease.

4.2.2 Incontinence score questionnaire

The severity of faecal incontinence was graded with the validated St Mark's Incontinence Score (Vaizey et al. 1999) which takes into account consistency and frequency of anal incontinence (gas, liquid solid) and its effect on lifestyle, the need to wear a pad or plug, the use of constipating medication and the lack of ability to defer defecation for 15 minutes (appendix 2). The types of anal incontinence and its effect on lifestyle are scored from 0 (never) to 4 (daily), the need to wear pads and the use of medication 0 (no) or 2 (yes), and faecal urgency 0 (no) or 4 (yes) giving a total score of 0 (complete continence) to 24 (complete incontinence).

All 44 study participants were symptomatic with a mean and median St Mark's Incontinence Score of 4.1 and 3 respectively (range 1-12). Incontinence to stool was

present in 2 women (5%), and flatus incontinence occurred in 35 women (80%). Faecal urgency occurred in 15 women (34%). Of all these women 19 (43%) expressed some form of impact on daily living.

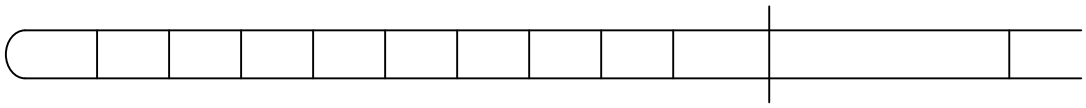
4.2.3 Vaginal manometry

Prior to performing vaginal manometry each participant underwent a vaginal examination carried out by myself, the principle investigator, to ensure correct contraction of the puborectalis muscle. The participant was instructed to 'squeeze the muscle used to stop the flow of urine midstream' whilst simultaneous vaginal examination was done.

Vaginal pressures were recorded using an 18 channel water perfused manometry catheter with the subject in the supine position. The catheter was 4.42mm in diameter with the pressure sensitive part of the catheter being 7 cm in length. Pressure ports were placed at the same axial level of the catheter in pairs 180 degrees apart such that ports 1 and 2, 3 and 4, 5 and 6, 7 and 8 were located at approximately 0 and 180 degrees i.e. antero-posteriorly and at 1cm to 3.25 cm from the cervix and ports 9 and 10, 11 and 12, 13 and 14, 15 and 16 and 17 and 18 were located at approximately 90 and 270 degrees i.e. laterally and at 4cm to 7cm from the cervix. The first pair of pressure ports (1 and 2) were located at 1cm from the tip of the catheter with each pair of ports thereafter placed at 7.5mm apart (figure 4.1). The catheter had a longitudinal reference line along the length of the catheter on the posterior side (180 degrees) to ensure the catheter was placed with consistent orientation in all subjects. After zeroing the catheter at the level of the vaginal introitus the catheter was inserted into the vagina. Pressures were displayed in cm H20 and recorded onto a department computer using the software programMedical Measurements System (MMS; http://www.mmsinternational.com/int/). Measurements were obtained at rest, during cough and maximum pelvic floor (squeeze) contraction with measurements being repeated 3 times for each subject. Examples of the vaginal manometry trace acquired during rest, cough and squeeze of the pelvic floor for one study subject and one control are shown in figures 4.2 and 4.3. For comparison purposes an example vaginal manometry trace from a nulliparous control at rest and during squeeze from similar work carried out by Guaderrama et al. 2005 is shown in figure 4.4.

Figure 4.1 Vaginal manometry catheter design a) longitudinal view b) cross-sectional view.

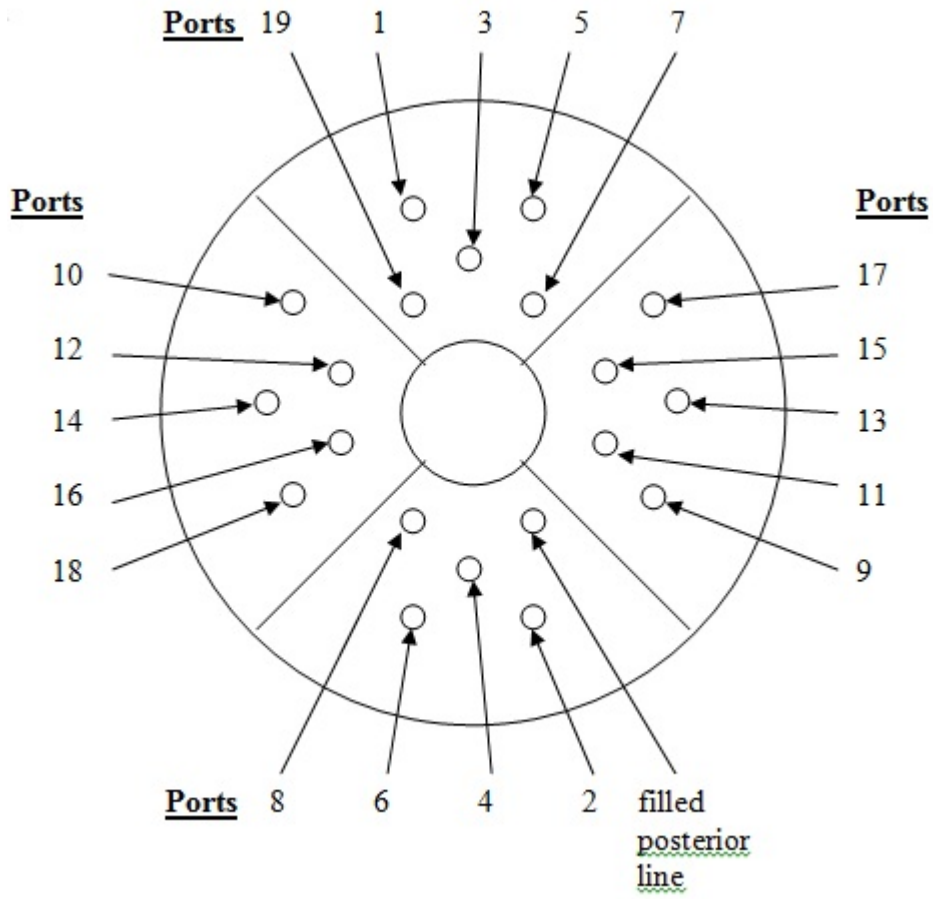
a) Longitudinal view



1	3	5	7	9	11	13	15	17	**Vaginal**	19
2	4	6	8	10	12	14	16	18	**Introitus**	

Each pair of ports placed at 0.75cm intervals
Distance from tip of catheter to ports 1 & 2 = 1cm

b) Cross-sectional views



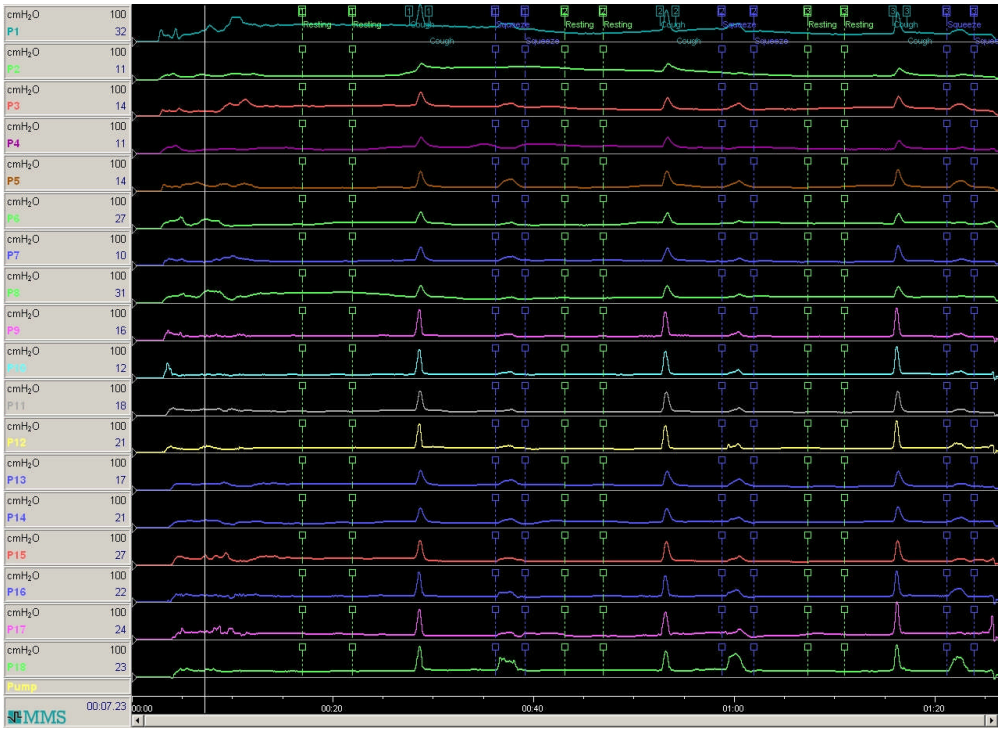


Figure 4.2 – An example of a vaginal manometry tracing from one patient during rest, cough and squeeze repeated 3 times.

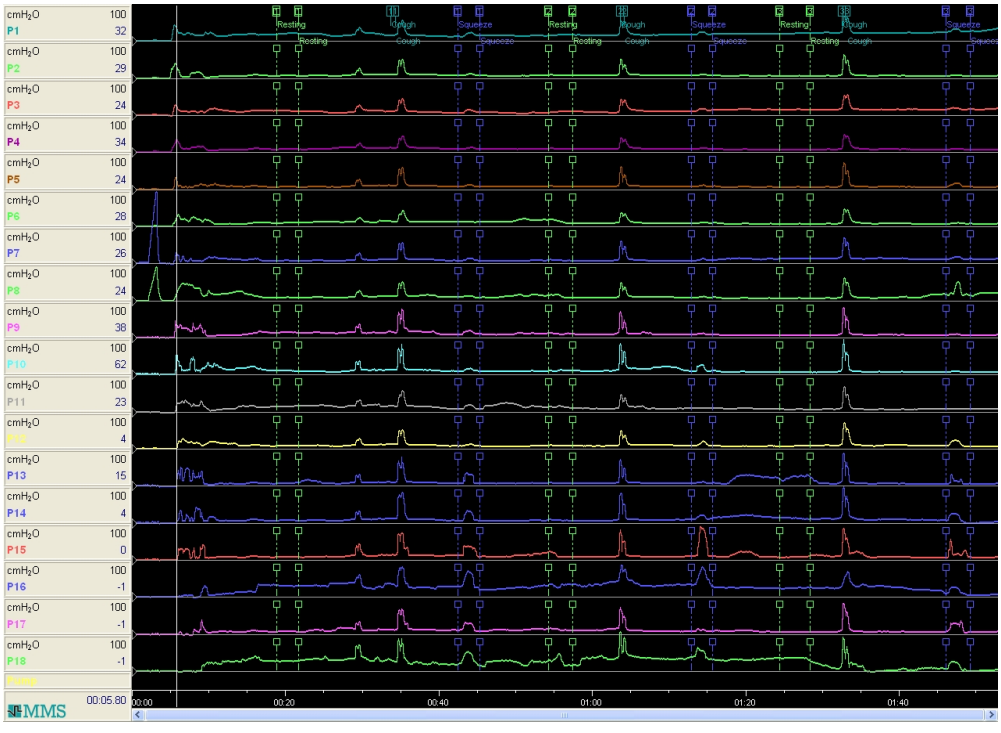


Figure 4.3 – An example of a vaginal manometry tracing from one control during rest, cough and squeeze repeated 3 times.

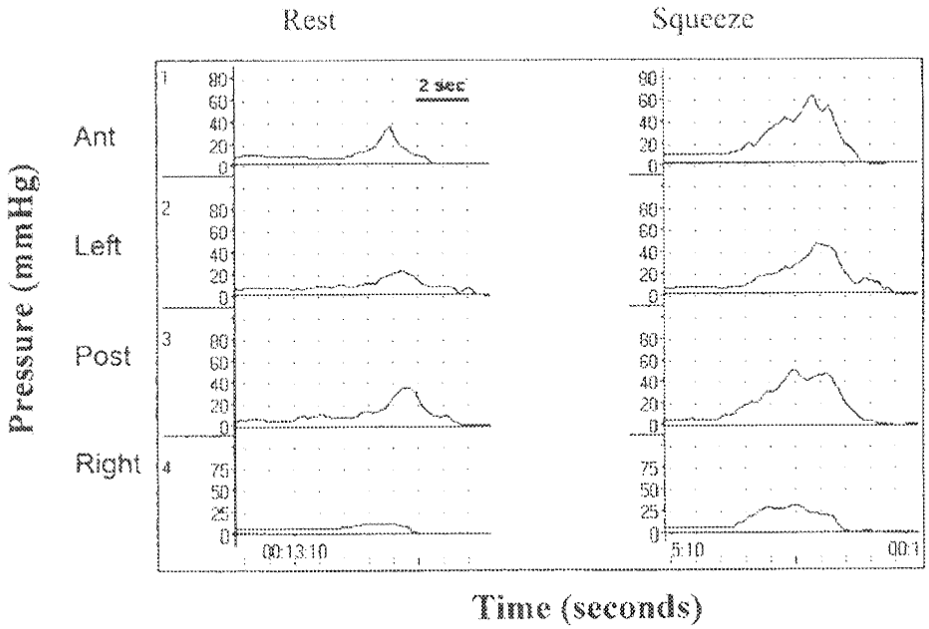


Figure 4.4 – An example of a vaginal manometry tracing from one nulliparous subject at rest and during squeeze attained by Guaderrama et al. 2005.

In order to alter the location of the pressure ports along the vaginal canal, the vaginal manometry catheter was then rotated 90 degrees clockwise in 13 study group participants resulting in ports 1-8 lying in the 90 and 270 degree orientation i.e. laterally and ports 9-18 in the 0 and 180 degree orientation i.e. antero-posteriorly (figure 4.5 and 4.6) and the same measurements recorded 3 times.

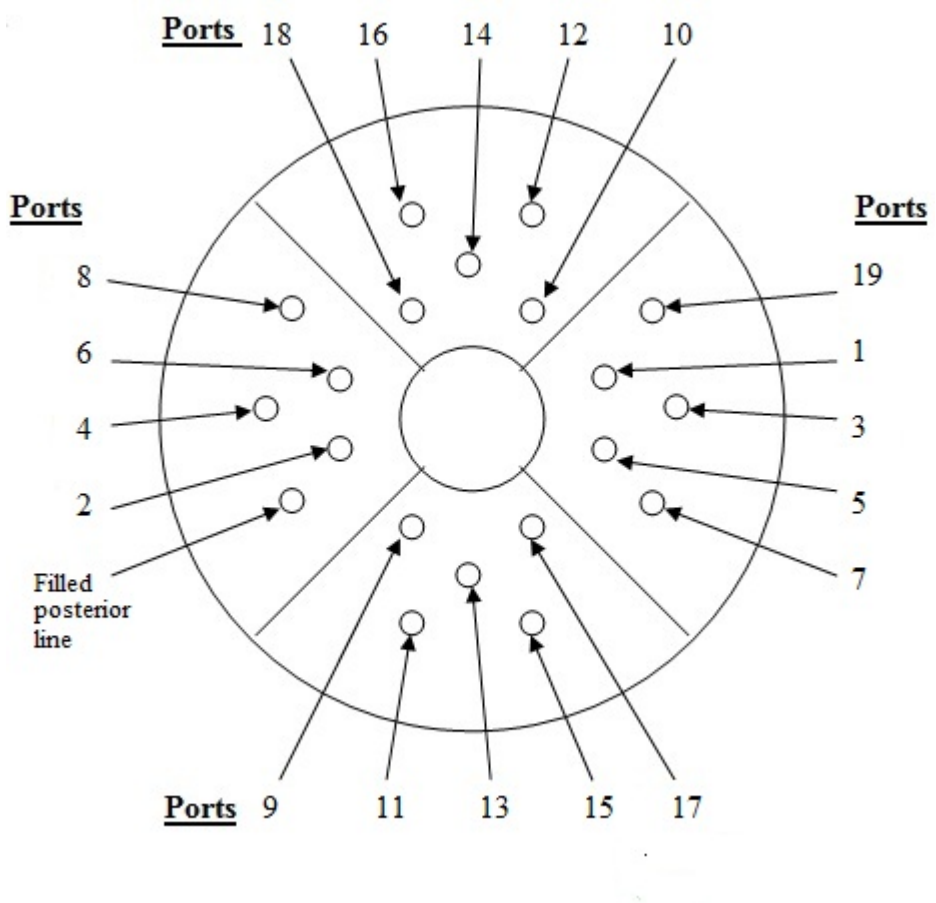


Figure 4.5 Configuration of pressure ports following 90 degree clockwise rotation of the vaginal manometry catheter.

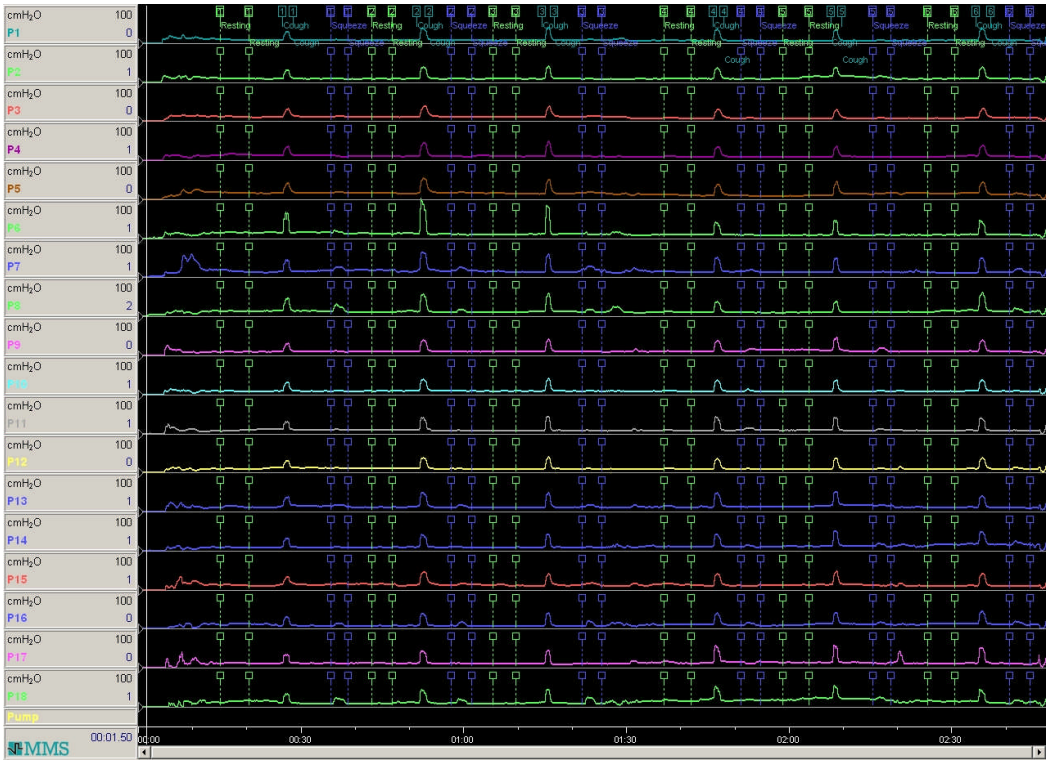


Figure 4.6 – An example of a vaginal manometry tracing from one study participant during rest, squeeze and cough with 90 degree rotation of catheter.

4.2.4 Anorectal manometry

Manometric assessment of the anal sphincter was performed with the patient positioned in the left lateral position using a balloon tipped water perfused catheter with 8 radially arranged ports lying 5 cm from the tip. The software program Medical Measurements System (MMS; http://www.mmsinternational.com/int/) was used for data acquisition.

The catheter was inserted into the rectum and the functional anal canal length was firstly defined by withdrawing the catheter until the high pressure zone of the anal canal was identified. A 1cm station pull through technique commencing at 6cm from the anal verge was then used to measure firstly the mean maximal resting pressure followed by the mean maximal incremental squeeze pressure (i.e. the mean maximal increase above the resting pressure). Measurements were repeated only once for each subject.

4.2.5 Statistical analysis

The maximum resting pressure and maximum incremental squeeze pressure at ports 1-8 and ports 9-18 from the 3 recordings from each participant was calculated and then

averaged giving a final mean maximal resting pressure and mean maximal incremental squeeze pressure. Data was tested for normality using the Kolmogorov-Smirnov test and presented as median and interquartile range or mean and standard deviation for continuous data.

The statistical significance of differences for the mean maximal resting pressure and mean maximal incremental squeeze pressure measured at the antero-posterior ports and lateral ports firstly between the control nulliparous group and obstetric anal sphincter tear group and secondly following 90 degree clockwise rotation of the vaginal manometry catheter were determined using the two sample t-test or Mann-Whitney U test where appropriate. To assess for intra-subject variability of the rest and squeeze measurements recorded at ports 1-8 and 9-18 the intraclass correlation coefficient (ICC) was calculated. The Bland Altman Method of Agreement (Bland and Altman 1986) was used in this study to assess for agreement between the established technique for the measurement of anal sphincter squeeze pressure, anorectal manometry and the newly proposed measurement technique, vaginal manometry therefore determining replacement of the old anorectal manometry method by the new vaginal manometry method. The data for subjects and controls were combined as one group for assessment of intra-subject repeatability and agreement between vaginal manometry and anorectal manometry in the measurement of squeeze pressure.

Statistical analyses were performed using SPSS version 19 (SPSS Inc., Chicago, IL, USA). A P-value of less than 0.05 was considered to be statistically significant in all analyses. The intraclass correlation coefficient values were interpreted as <0.2, poor agreement; 0.3-0.4, fair agreement; 0.5-0.6, moderate agreement; 0.7-0.8, strong agreement and >0.8, almost perfect agreement (Altman 1999).

4.3 Results

I could not reproduce the previously described presence of three distinct vaginal pressure zones (proximal, mid and distal) in either the control or patient groups with the use of vaginal manometry as previously described.

Table 4.1 demonstrates the vaginal pressures recorded during rest and squeeze in the control and study groups. In the control group, the mean maximal resting pressure was

significantly higher in the lateral ports in comparison to the study group (25.6cm H_20 vs 17.3cm H_20 p<0.001). The controls were also found to have a significantly higher mean maximal incremental squeeze pressure along the whole length of the vaginal canal in comparison to the study group (ports 1-8 15.3cm H_20 vs 8.1cm H_20 p<0.001; ports 9-18 28.2cm H_20 vs 17.3cm H_20 p=0.001). At rest, there was a significant difference in the mean pressures recorded between the antero-posterior and lateral ports (p=0.006) in the control group only. During squeeze, the mean pressures recorded were found to be approximately twice as high in the lateral ports compared to the antero-posterior ports in both the study (p<0.001) and control (p=0.003) group.

	Controls (n=14)	**Study subjects (n=44)**	**p value**
Mean maximal resting pressure (cm H_20)			
Ports 1-8 (antero-posterior)	18.4 (5.8)	16.8 (5.4)	0.34
Ports 9-18 (lateral)	25.6 (8.2)	17.3 (4.1)	<0.001
Mean maximal incremental squeeze pressure (cm H_20)			
Ports 1-8 (antero-posterior)	15.3 (9.6)	8.1 (5)	<0.001
Ports 9-18 (lateral)	28.2 (17.2)	17.3 (7.7)	0.001

Table 4.1 Vaginal manometry measurements in nulliparous controls and primiparous study group. Values expressed as mean (SD). T-test.

There was no significant difference in the pressures generated with the catheter in the original configuration compared to rotation of the catheter 90 degrees clockwise during rest and squeeze (table 4.2).

	Catheter in original configuration (n=13)		Catheter rotated 90 degrees clockwise (n=13)	p value
Mean maximal resting pressure (cm H_20)				
Ports 1-8 (antero-posterior)	16 (4.3)	Ports 1-8 (lateral)	15.7 (3.4)	0.85
Ports 9-18 (lateral)	17.9 (4.4)	Ports 9-18 (antero-posterior)	20.6 (5.3)	0.17
Mean maximal incremental squeeze pressure (cm H_20)				
Ports 1-8 (antero-posterior)	7 (8.6)	Ports 1-8 (lateral)	6.6 (3)	0.76
Ports 9-18 (lateral)	17.9 (8.6)	Ports 9-18 (antero-posterior)	24.7 (19.9)	0.27

Table 4.2 Vaginal manometry measurements with catheter in original configuration and 90 degree clockwise rotation. Values expressed as mean (SD). T-test.

There was poor agreement between anorectal and vaginal manometry in the measurement of pelvic floor squeeze as demonstrated by the Bland-Altman plots (figures 4.7 and 4.8).

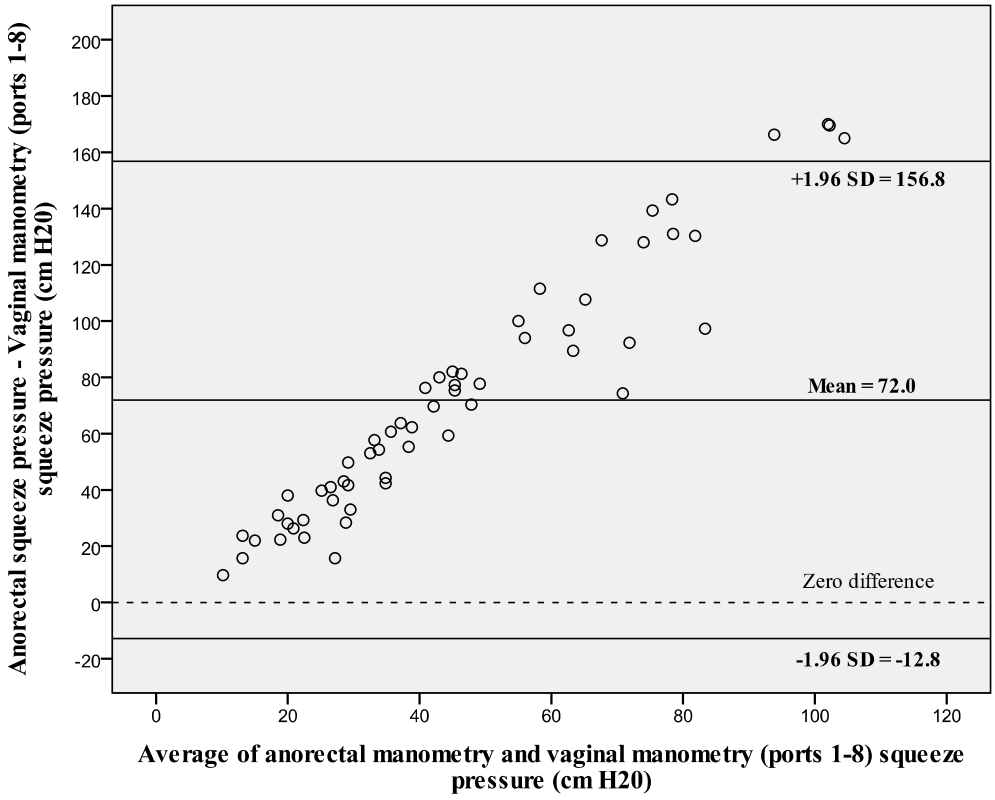


Figure 4.7 - Bland Altman plot assessing agreement of anorectal manometry and vaginal manometry (ports 1-8) in the measurement of maximal incremental squeeze pressure in all subjects (14 nulliparous, 44 acute tears).

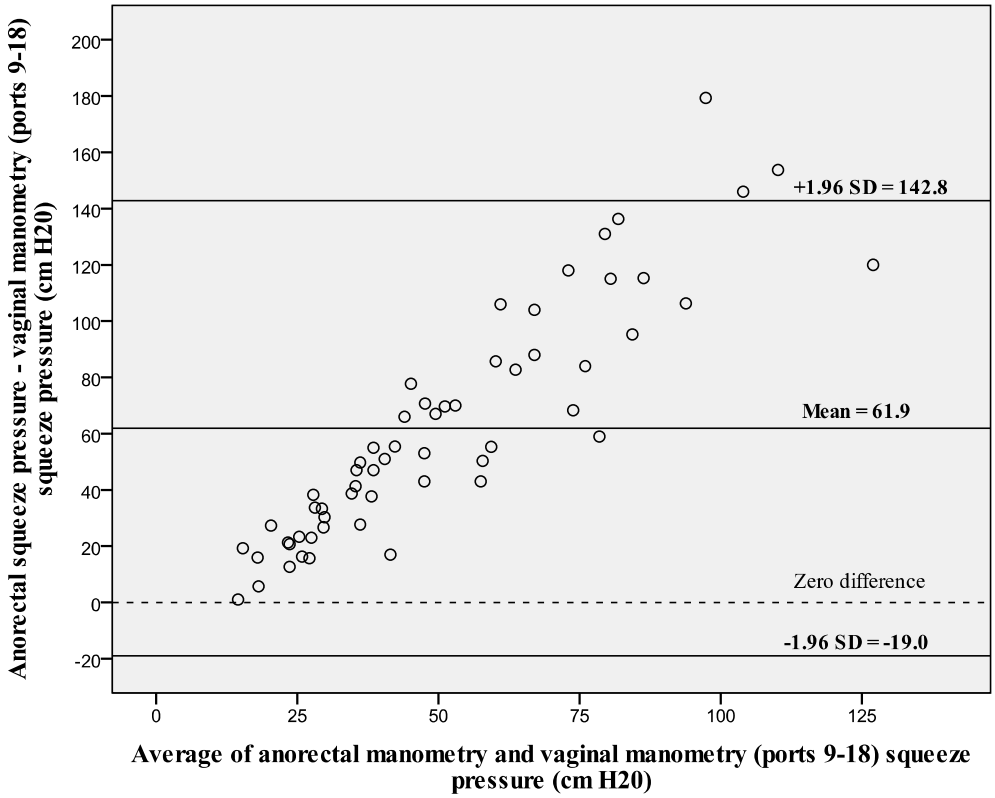


Figure 4.8 - Bland Altman plot assessing agreement of anorectal manometry and vaginal manometry (ports 9-18) in the measurement of maximal incremental squeeze pressure in all subjects (14 nulliparous, 44 acute tears).

An incidental observation made during the study was the generation of an identical pressure wave along the full length of the vaginal canal in both control and study subjects during cough (figures 4.9, 4.10, 4.11, 4.12), implying the possibility that cough is actually a measure of pelvic floor muscle contraction and not intra-abdominal pressure.

Figures 4.9, 4.10, 4.11, 4.12 Examples of vaginal canal pressures recorded during cough in controls and study subjects

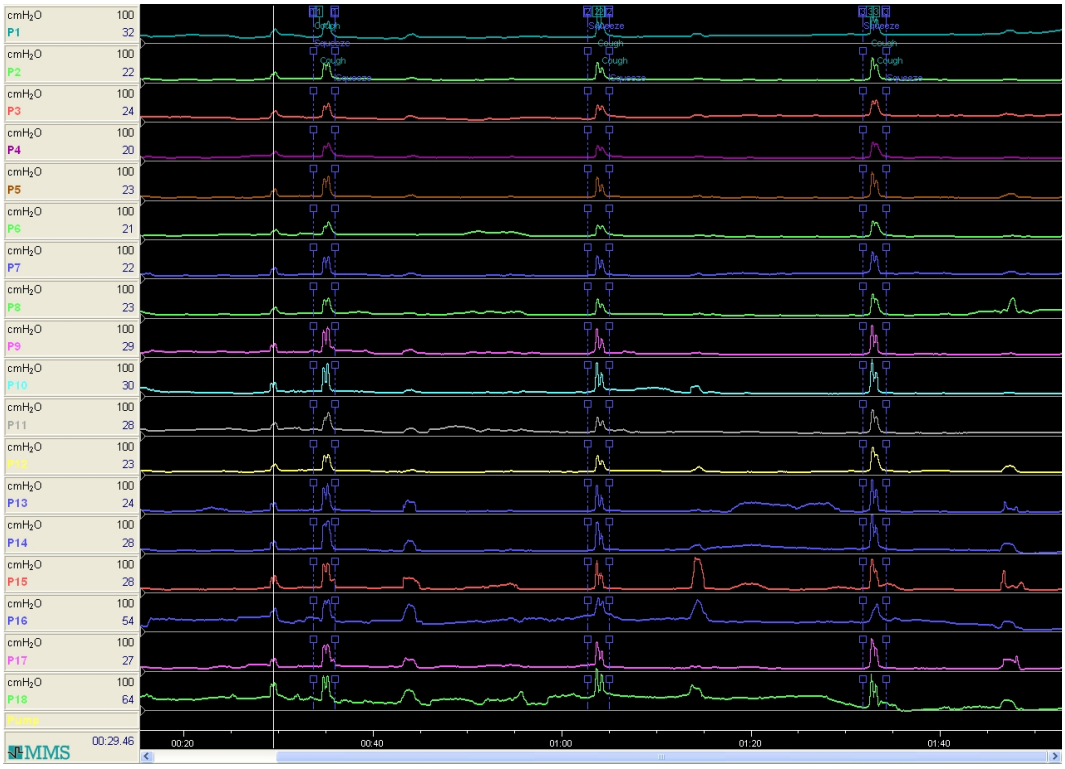


Figure 4.9 Control

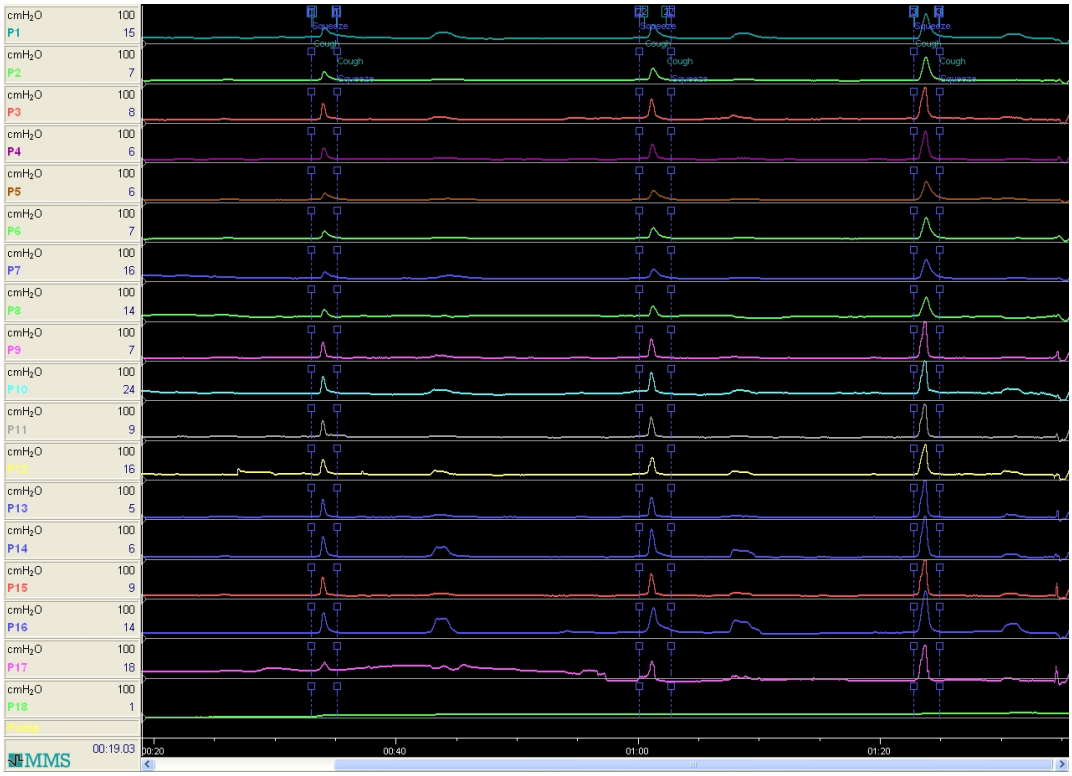


Figure 4.10 Control

Figure 4.11 Study participants

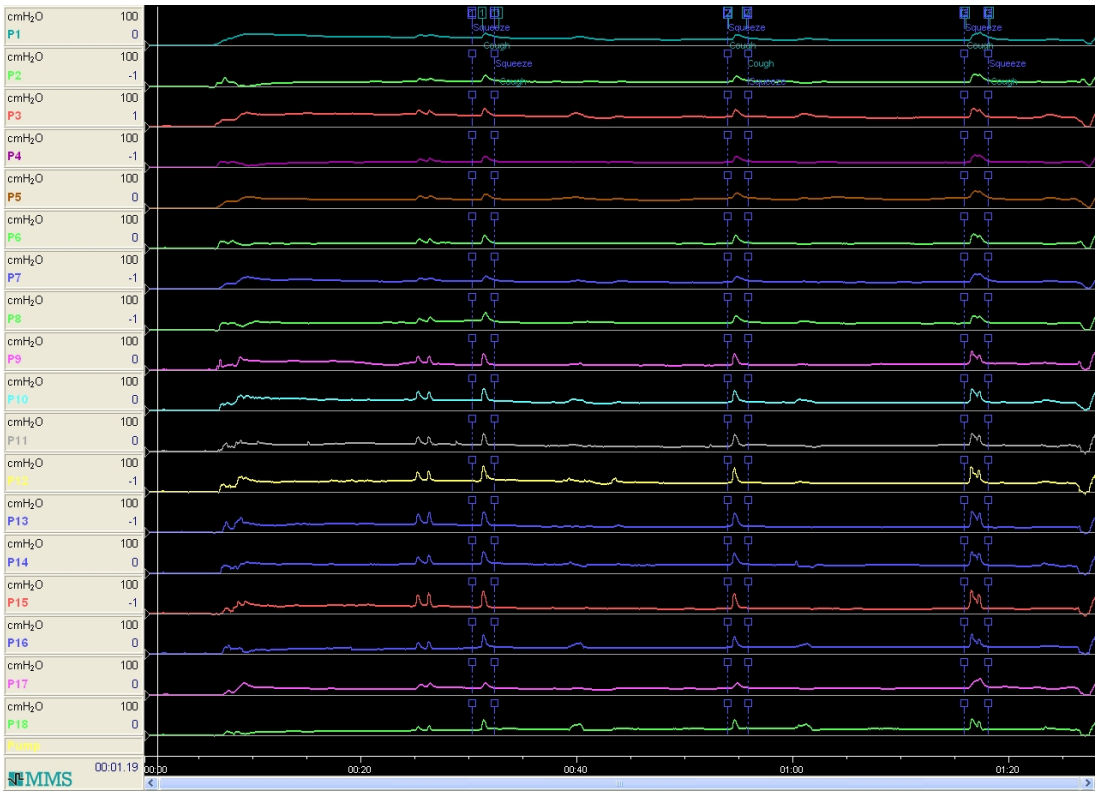


Figure 4.12 Study participants

The intraclass correlation revealed moderate agreement with repeated measurements in both ports 1-8 for rest (ICC=0.68 95% CI 0.55-0.78) and squeeze (ICC=0.61 95% CI 0.47-0.73) and ports 9-18 for rest (ICC=0.69 95% CI 0.57-0.79) and almost perfect agreement with repeated measurements in ports 9-18 for squeeze (ICC=0.81 95%CI 0.73-0.88).

4.4 Discussion

The goal of the present study was two fold: firstly to define the vaginal pressure profile in symptomatic women with acute obstetric anal sphincter tears in comparison to healthy nulliparous controls using vaginal manometry, and secondly to assess the agreement between anorectal and vaginal manometry in the measurement of squeeze pressure.

To my knowledge this is the first study to define the vaginal pressure profile in pathological patients in comparison to control patients using water perfused vaginal manometry. The presence of three distinct pressure zones within the vaginal canal has previously been hypothesised by an American research group (Guaderrama et al. 2005) to be anatomically placed above, at the level of and below the pelvic diaphragm depicting intra abdominal, pelvic floor squeeze and atmospheric pressure respectively. My study showed that the vaginal canal contains neither a uniform pressure zone nor the presence of any distinct zones. Although my catheter design was different to that used by Guaderrama et al. 2005 both systems were essentially water perfused hence measuring precise absolute pressure. In addition the length of my catheter was 7cm with each pair of perfusion pressure ports being placed at 0.75cm apart therefore recording more data points in both the axial and longitudinal positions. Despite the vaginal canal being measured at approximately 10cm our vaginal manometry catheter will have spanned across all 3 proposed vaginal zones. However I was despite this unable to clearly demonstrate the presence of 3 distinct vaginal pressure zones as shown by Guaderrama et al. 2005. The anatomic correlates of the pressure ports were not determined in this study.

During pelvic floor contraction, a significantly larger squeeze pressure was generated along the whole length of the vaginal canal by the nulliparous controls in comparison to the incontinent patients. This observation would be in keeping with the hypothesis that

healthy nulliparous controls have structurally and functionally intact pelvic floor musculature. In both controls and patients, squeeze pressures tended to be greater in the distal part of the vaginal canal, in support of previous work (Kegel 1948; Bo 1992).

At rest, the pressures recorded in the distal part of the vaginal canal were significantly greater than the proximal part in the control group. However no significant difference was found in the rest and squeeze pressures generated between the anteroposterior- and laterally-placed ports in the same group.

Finally, the mean resting pressure recorded was greater than the mean squeeze pressure in the anteroposterior- or proximally-placed ports in the study group. This finding may be explained by the catheter being positioned non centrally within the vaginal canal and therefore making greater contact with the anterior or posterior wall during the rest. Despite these findings the squeeze and rest pressures recorded in my nulliparous group were overall still smaller than that recorded by Guaderrama et al. 2005 which may be due to incomplete mucosal contact being made with the manometry catheter therefore resulting in incomplete measurement of pressures, or due to greater fatiguability of the pelvic floor musculature with the use of the stationary method compared to the motorised pull through method utilised by Guaderrama et al. 2005. Schizas et al. 2011 looking at anorectal manometry, carried out a study to determine the optimal technique (station pull through vs slow and fast automated pull through) to measure anorectal rest and squeeze pressures in 24 healthy volunteers. They found a significant variation between the values recorded by the two methods; the squeeze and rest pressures recorded by the stationary pull through technique were significantly lower than that calculated by the high speed (25 mm/s) automated pull through technique. The authors accounted this difference to the element of fatigue of the anorectal muscles by the time the catheter was within the functionally significant region of the anal canal. Rotation of the catheter 90 degree clockwise resulted in a higher rest and squeeze pressure in ports 9-18 (now antero-posteriorly positioned) which although did not reach statistical significance supports the results presented by Guaderrama et al. 2005 and Raizada et al. 2010 and ensured the catheter was not locked.

Classical understanding of anal canal physiology states that the tonically active internal anal sphincter contributes to the majority (85%) of the resting anal sphincter pressure

with the external anal sphincter contributing the remainder. The external anal sphincter is held to be primarily responsible for voluntary squeeze with the puborectalis muscle enhancing faecal continence by maintenance of the anorectal angle. Up until recently, the role puborectalis muscle plays within the actual formation of anal canal pressure has not been completely understood. Using simultaneous anal manometry and three-dimensional endovaginal ultrasonography to study the functional correlates of anal canal anatomy, Liu et al. 2006 showed that proximal anal canal squeeze pressure was entirely due to puborectalis muscle contraction and distal squeeze pressure was secondary to external anal sphincter contraction. Hence highlighting the dual role puborectalis muscle plays in maintaining continence and providing organ support through constrictor and elevator function respectively. They also demonstrated circumferential asymmetry in the proximal anal canal pressure representing the 'u' shaped sling of the puborectalis muscle and, circumferential symmetry in the distal anal canal representative of the circular shaped external anal sphincter (Liu et al. 2006). Based on this finding I attempted to look at the relationship between vaginal and anorectal manometry in the measurement of pelvic floor squeeze and found very poor agreement. One possible explanation could be that vaginal manometry measures pelvic floor muscle squeeze as a whole and as yet it is not completely understood what individual muscles of the levator ani contribute to the genesis of the squeeze pressure where as anorectal manometry purely measures puborectalis muscle squeeze in the proximal anal canal. Secondly, I did not use imaging to locate the precise anatomical position of the puborectalis and external anal sphincter along the anal canal and therefore it was impossible to know whether the circumferential mean maximum incremental squeeze pressure measured by anorectal manometry was generated by the puborectalis muscle or the external anal sphincter. One can therefore conclude that in everyday clinical practice the use of anorectal manometry to measure puborectalis muscle strength and its contribution to anorectal squeeze pressure is limited unless undertaken simultaneously with three-dimensional ultrasonography to determine the precise anatomical correlates within each individual.

One of the most revealing findings in my study was the pressure wave generated with vaginal manometry during voluntary cough. Voluntary coughing involves synchronised contractions of the thoracic, abdominal and pelvic floor muscles along with coordinated rectal and urethral closure resulting in an increase in intra-abdominal pressure and

prevention of incontinence (Addington et al. 2008). Previous urodynamic studies have used vaginal pressure measured above the urogenital diaphragm as a surrogate marker of intra abdominal pressure (Richardson 1985, Wall et al. 1995). Whilst vaginal pressure measurements can produce low pressure motion artifact and be less securely placed compared to previously used rectal pressure measurement, low amplitude vaginal contractions occur less frequently than high pressure spontaneously occurring rectal contractions. In my study voluntary cough produced a pressure wave which was symmetrical around the vaginal canal and along the full length of the vagina at a magnitude of approximately 3 to 4 fold from the baseline. This pattern was seen consistently in *all* study subjects and controls, making it a highly reproducible observation. It may be questioned if this cough pressure wave was a result of movement artefact however this is unlikely as the baseline was stable in all study subjects with no variations. Following rotation of the catheter 90 degrees clockwise the same phenomenon was seen. One can conclude that the intra abdominal pressure is not being measured by this method due to the resulting transmitted abdominal pressure wave around and along the length of the vaginal canal with cough. It is possible that cough is reflective of pelvic floor muscle contraction with closure of the vaginal cavity instead of a measure of intra abdominal pressure.

One possible confounder to the vaginal pressure measurements obtained in this study is that study participant selection was purely based on being symptomatic with a clinical diagnosis of an obstetric anal sphincter tear and no endoanal ultrasound confirmation which may have identified subjects with an intact anal sphincter but who are symptomatic as a result of pudendal neuropathy. Secondly, the severity of symptoms varied amongst the study group which could have been a result of pure anal sphincter injury, pelvic floor muscle avulsion or rupture, pudendal neuropathy or a combination of any of these three. Thirdly, I included a mixture of breastfeeding and non breastfeeding study subjects which may have resulted in poor pelvic floor squeeze secondary to low oestrogen levels and hence inactive pelvic floor oestrogen receptors. Finally, despite using a standardised protocol throughout the study, subjects may still have used surrounding muscles such as gluteus, hip adductors and external rotator muscles when squeezing the pelvic floor which have all been shown to affect the intra-vaginal pressure (Bo et al. 1990; Peschers et al. 2001).

CHAPTER FIVE

A NOVEL QUANTIFICATION OF PELVIC FLOOR ATROPHY: VALIDATION OF TECHNIQUE AND ITS UTILITY IN FAECAL INCONTINENCE

5.1 Introduction

Since physiological measures have not been impressive as demonstrated by the results presented in chapters 3 and 4 the next imperative step is to determine whether more sophisticated measures may better reflect function and symptoms.

As discussed previously, anal sphincter trauma and pudendal nerve injury during childbirth is the commonest cause of faecal incontinence in women (Kamm 1994). Endoanal ultrasound (EAUS) has identified persistent defects in up to 85% of women following primary repair (Sultan et al. 1994). Although surgical anterior anal sphincter repair can be performed on symptomatic women with sphincter defects, the long term failure rates can be as high as 50% (Malouf et al. 2000). It has since been suggested that the presence of pudendal nerve damage leading to subsequent denervation and atrophy of the external anal sphincter (EAS) at the time of surgical repair is associated with poor outcome (Briel et al. 1999; Gilliland et al. 1998; Jacobs et al. 1990, Londono-Schimmer et al. 1994). Neurophysiological testing of neuropathy is undertaken either by measurement of pudendal nerve terminal latency (PNTML) which is non-physiological and unreliable or by electromyography (EMG) which is uncomfortable and only allows limited sampling of the sphincter (Williams et al. 2001).

Imaging modalities, notably endoanal ultrasound and pelvic MRI play an essential role in the assessment of incontinent patients, assessing both anal sphincter integrity and structure. Both MRI and EAUS have reported high accuracy for sphincter defects (Law et al. 1991; Cuesta et al. 1995; Nielsen et al. 1993; Deen et al. 1993; Meyenberger et al. 1996; deSouza et al. 1996; deSouza et al. 1995; Rociu E et al. 1999). Evaluation of sphincter quality is however less clear cut. MRI using either an endocoil or external surface coil is likely to be superior to EAUS although there is as yet no universal score or grading system available for the radiological diagnosis of EAS atrophy (Terra et al. 2006; Briel et al. 1999; Rociu et al. 1999; Williams et al. 2001; deSouza et al. 1996; Briel et al 2000; Fletcher et al. 2003). Quantitative measurement of percentage muscle fat content using endocoil MRI is however able to identify EAS atrophy (Terra et al. 2006; Williams et al. 2001; Briel et al. 2000; Briel et al. 1999).

More recently MR spectroscopy has been used to non-invasively quantify lipid content of muscle tissue (Boesch et al. 1997, Schick et al. 1993; Szczepaniak et al. 1999, Kreis

et al. 1996; Schick et al. 2002; Chatoor et al. 2009) and has been advocated as a more accurate measure of atrophy than the current subjective qualitative grading of T2 MR images. However, whilst MR spectroscopy appears robust for fat fraction measurement in larger muscles its use in smaller structures such as the EAS is less clear, notably due to contamination by adjacent fat inadvertently included in the minimum voxel size required for robust spectroscopic data collection. In such a situation another form of MR imaging such as the two point Dixon MRI technique may be more appropriate (Dixon 1984). This technique described in 1984 uses a two point chemical shift based water fat separation method allowing the calculation of the fat fraction in a marked region of interest therefore obviating the need for voxel placement within smaller muscles and structures. Recent validation of this technique against histopathology findings and MR spectroscopy have shown excellent agreement in the quantification of intrahepatic fat (Kim et al. 2008; Cali et al. 2009). Methods of assessing fat fraction such as the 2 point Dixon which do not rely on a minimum measurement voxel size may have utility in assessing small volume structures such as the pelvic floor and anal sphincter, although to date there is little data supporting their use.

The objectives of this prospective study were twofold. Firstly, to validate the use of the 2 point Dixon fat water decomposition technique against the gold standard MR spectroscopy in quantifying fat atrophy and thereafter to compare with subjective atrophy grades, anorectal manometry and incontinence scores in asymptomatic controls and subjects with idiopathic or obstetric trauma related faecal incontinence.

5.2 Methods

5.2.1 Validation of 2 point Dixon fat water decomposition MR imaging technique against MR spectroscopy in the quantification of muscle fat

5.2.1.1 Participants

This prospective study was performed at University College Hospital, London and consisted of 9 healthy nulliparous women and 1 healthy male (mean age 27 years, range 23-39 years) who were recruited by advertisement via webmail to employees working within the trust and students enrolled at the affiliated University College London. The study was approved by The National Hospital for Neurology and Neurosurgery and

Institute of Neurology Research Ethics Committee (10/H0716/10) and written consent was obtained from all participating subjects.

Exclusion criteria for controls were a history of anorectal surgery, childbirth, subjects less than 18 years of age, medical co morbidities affecting bowel function i.e. diabetes, endocrine disease, scleroderma, and inflammatory bowel disease.

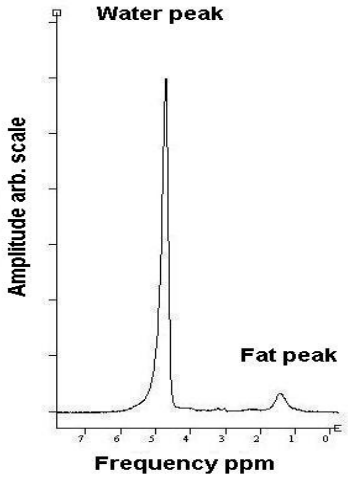
5.2.1.2 MR imaging

MR images were obtained using the 1.5T Avanto MR system (Siemens Healthcare, Erlangen Germany) with an external flexible body coil. T2-weighted spin echo images of the pelvis were acquired in the transverse plane. Identically positioned fat and water images were obtained using a 3D VIBE gradient echo sequence incorporating a two point Dixon technique (TR 11.1ms, TE 4.76/7.14ms, slice thickness 3.3mm) that generated fat and water images with a Siemens proprietary algorithm.

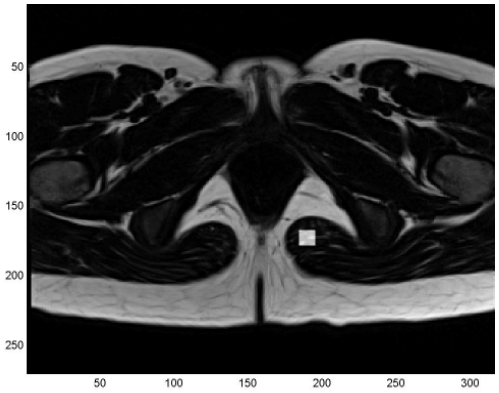
Proton MRS was performed using Point Resolved Spectroscopy (PRESS; TR 5000ms, TE 30ms and 50ms). A 10mm cubic voxel was positioned within the left medial side of the gluteus maximus muscle at the site of the largest diameter on the axial T2 weighted images by the principle researcher (DP). The PRESS acquisition was divided into 10 subspectra which were later summed by an experienced MR physicist. All 10 controls were then asked to get off the scanner table and stand up for 5 minutes; the controls were then repositioned on the scanner table and the full examination repeated. The second voxel was placed by the same principle researcher within the same site of the left gluteus maximus muscle; no attempt to reproduce the previous voxel position was made so these were later treated as separate measurements.

Offline spectroscopy analysis was performed using the JMRUI package (Stefan et al. 2009). Fat and water spectral peaks were fitted using the AMARES algorithm to provide peak amplitudes at 30 ms and 50 ms (Stefan et al. 2009). The acquisition of two echo times allowed for a correction for T2 effects by assuming a mono-exponential decay of fat between 30 and 50 ms. Spectroscopy fat fractions were obtained by dividing the T2-corrected (t=0) fat peak amplitude by the sum of the T2-corrected fat and water peak amplitudes (figure 5.1).

Figure 5.1 a) Proton MR spectroscopy spectrum of the gluteus maximus in a nulliparous control. b) Transverse T2-weighted spin echo MR image with spectroscopy voxel marked in the left medial gluteus maximus. c) Corresponding colour coded fat fraction map of voxel calculated from 2 point Dixon fat and water images.



a)



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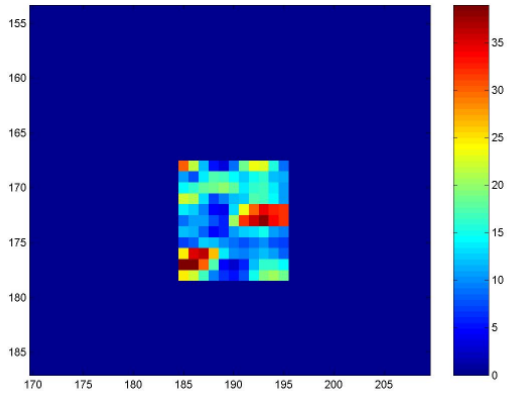


c)

Water and fat images were processed using MATLAB. The fat fractions were produced by dividing the fat images by the sum of the fat and water images (x 100%). The spectroscopy voxel was then localised as a 10 x 10 mm region of interest (ROI) on the fat fraction maps and a mean value calculated over the three slices of interest (3 x 3.3 ≈10 mm).

5.2.1.3 Data Analysis

The Bland-Altman method (Bland and Altman 1986) was used to assess the agreement between the two MR techniques in quantifying muscle fat content.

5.2.2 Application of 2 point Dixon fat water decomposition MRI in the quantification of the anal sphincter complex in healthy controls and incontinent patients

5.2.2.1 Participants

This prospective study was performed between February 2011 and August 2011 at University College Hospital, London. The study group consisted of 19 consecutive female patients (mean age 52, range 31-75 years) referred to the GastroIntestinal Physiology Unit with symptoms of idiopathic or post-obstetric trauma faecal incontinence. Eight of these study subjects had sonographically confirmed third or fourth degree obstetric anal sphincter tears which were all well repaired with no evidence of residual defects. The remainder of subjects had idiopathic or chronic obstetric related trauma with external anal sphincter and/or puborectalis muscle atrophy visualised on endoanal ultrasound performed by two GI radiologists with over 10 years of experience.

The control group consisted of 12 healthy nulliparous women and 1 healthy male (mean age 30, range 23-39 years) who were recruited by advertisement via webmail to employees working within the trust and students enrolled at the affiliated University College London. Ten of the controls within this group were included in the initial validation study. The study was approved by The National Hospital for Neurology and Neurosurgery and Institute of Neurology Research Ethics Committee (10/H0716/10) and written consent was obtained from all participating subjects.

Exclusion criteria for both controls and study subjects were a history of anorectal surgery, childbirth, subjects less than 18 years of age, medical co morbidities affecting bowel function i.e. diabetes, endocrine disease, scleroderma, and inflammatory bowel disease.

5.2.2.2 Design

All study participants had a full history taken with evaluation of incontinence symptoms with the St Mark's Incontinence Score (Vaizey et al. 1999) along with conventional MR

imaging and 2 point Dixon fat water decomposition MR imaging of the anal sphincter complex. All 19 incontinent patients and 8 of the 13 control subjects also underwent clinical examination and anorectal manometry.

5.2.2.3 Incontinence score questionnaire

The severity of faecal incontinence was graded with the validated St Mark's Incontinence Score (Vaizey et al. 1999; appendix 2) with a score range from 0 (complete continence) to 24 (complete incontinence). For analysis purposes the individual St Mark's Incontinence Score was divided into the following severity subgroups; mild (0-4), moderate (5-8) and severe (>8) (Roos et al. 2009).

5.2.2.4 Anorectal physiology

Manometric assessment of the anal sphincter was performed by the study coordinator with the patient positioned in the left lateral position using a balloon tipped water perfused catheter with 8 radially arranged ports lying 5 cm from the tip. The Medical Measurement Systems (MMS; http://www.mmsinternational.com/int/) software program was used for data acquisition.

The manometry technique is as previously described, in brief a catheter was inserted into the rectum and the functional anal canal length was firstly defined by withdrawing the catheter until the high pressure zone of the anal canal was identified. A 1cm station pull through technique commencing at 6cm from the anal verge was then used to measure firstly the mean maximal resting pressure followed by the mean maximal squeeze pressure (i.e. the mean maximal increase above the resting pressure). The rectoanal inhibitory reflex (RAIR) was also recorded followed by the rectal sensitivity which involved inflation of the balloon at the tip of the catheter with air to determine the volume (in millilitres) required to create the sensation of threshold, urge and maximum tolerated volumes.

Anal mucosal electrosensitivity was measured using a bipolar electrode probe (Galtec) which was introduced into the anal canal. A constant current (electrical stimulation of 5 HZ, along with a pulse width of 0.1msec was applied in the anal canal) was incrementally increased from 1 to 20 mA in the anus until the patient indicated the threshold of sensation.

5.2.2.5 MR imaging of anal sphincter complex

5.2.2.5.1 Controls

Ten of the controls who participated in the initial validation study were also included in the second part of the study; an additional three controls were recruited to take part in the second part of the study.

As previously mentioned, T2-weighted spin echo images (TR 4030ms, TE 96ms, slice thickness 3mm, slice gap 0.3mm) of the anal canal were acquired in the coronal and transverse planes using the 1.5T Avanto MR system (Siemens Healthcare, Erlangen Germany) with an external flexible body coil. Identically positioned fat and water images were obtained using a 3D VIBE gradient echo sequence incorporating a two point Dixon technique (TR 11.1ms, TE 4.76/7.14ms, slice thickness 3.3mm, 24 slices) that generated fat and water images with a Siemens proprietary algorithm. The full scanning sequence was repeated in 10 (those who took part in the initial validation study) of the 13 controls. Before repeating the full examination all 10 controls were asked to get off the scanner table, stand up for 5 minutes and then repositioned on the scanner table.

5.2.2.5.2 Study Participants

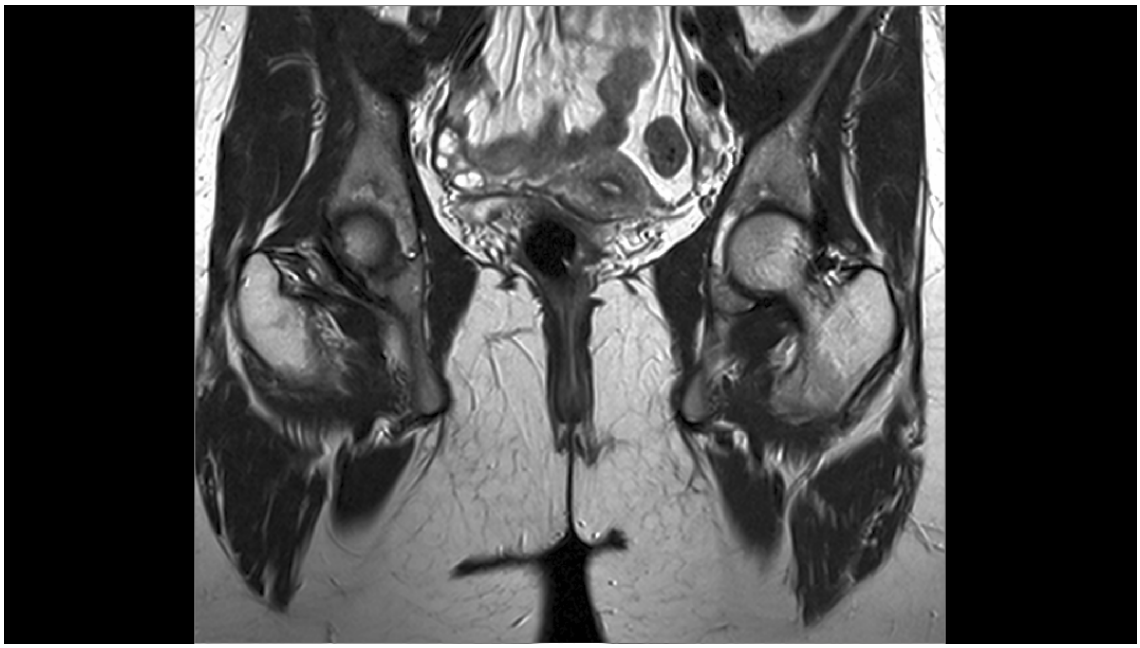
All 19 of the study participants underwent T2-weighted spin echo images (TR 4030ms, TE 96ms, slice thickness 3mm, slice gap 0.3mm) of the anal canal in the coronal and transverse planes using the 1.5T Avanto MR system (Siemens Healthcare, Erlangen Germany) with an external flexible body coil. Identically positioned fat and water images were obtained using a 3D VIBE gradient echo sequence incorporating a two point Dixon technique (TR 11.1ms, TE 4.76/7.14ms, slice thickness 3.3mm, 24 slices) that generated fat and water images with a Siemens proprietary algorithm.

5.2.2.6 Image analysis

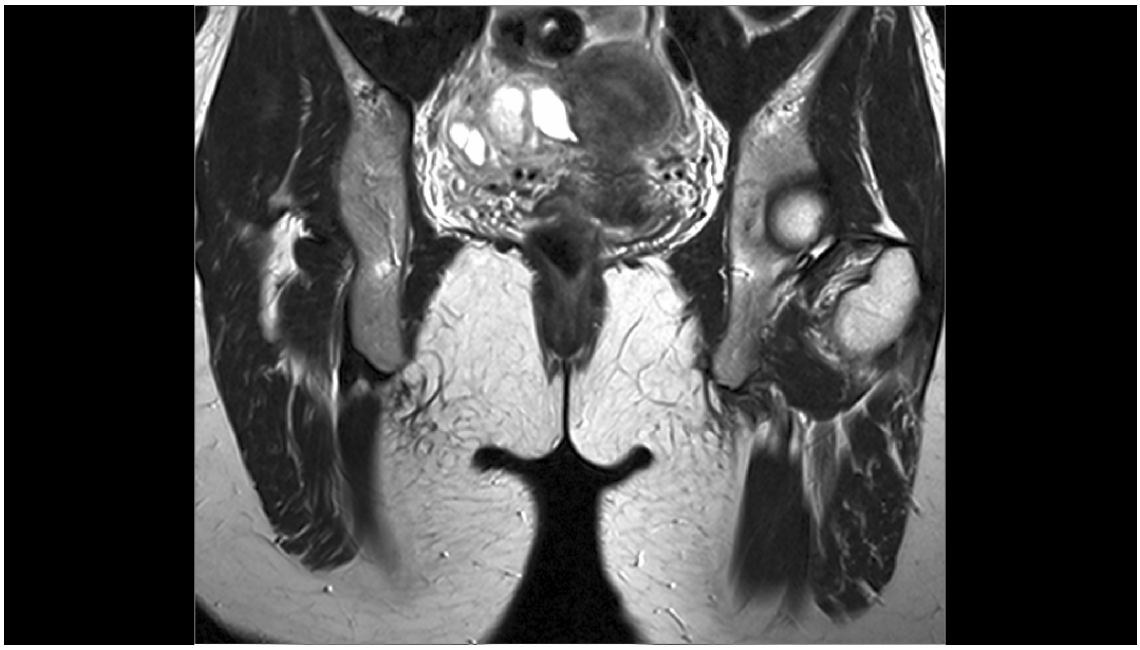
Two radiologists with 10 years experience in reading pelvic floor MRIs subjectively graded the degree of atrophy of the EAS and PRM from the T2 MR images (figure 5.2). Both radiologists were blinded to the clinical history, anorectal manometry findings and fat fraction images of the subjects. EAS and PRM atrophy were individually graded as 1 (no thinning or no replacement of muscle by fat), 2 (<50% thinning or replacement of muscle by fat) or 3 (>50% thinning or replacement of muscle by fat) (Terra et al. 06).

The grade of atrophy was based on the overall individual appearance of the EAS and PRM muscles.

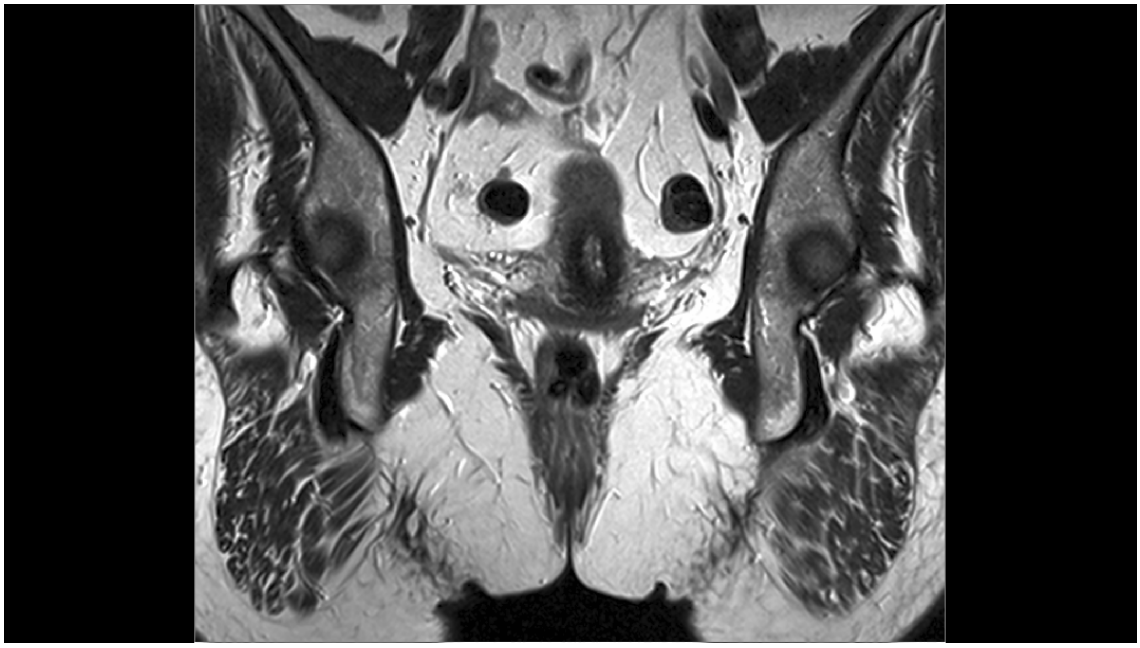
Figure 5.2 Coronal T2-weighted spin echo images of the anal canal demonstrating a) normal anatomy or grade 1 atrophy b) moderate or grade 2 atrophy c) severe or grade 3 atrophy of the external anal sphincter and puborectalis muscles.



a) Grade 1 atrophy



b) Grade 2 atrophy



c) Grade 3 atrophy

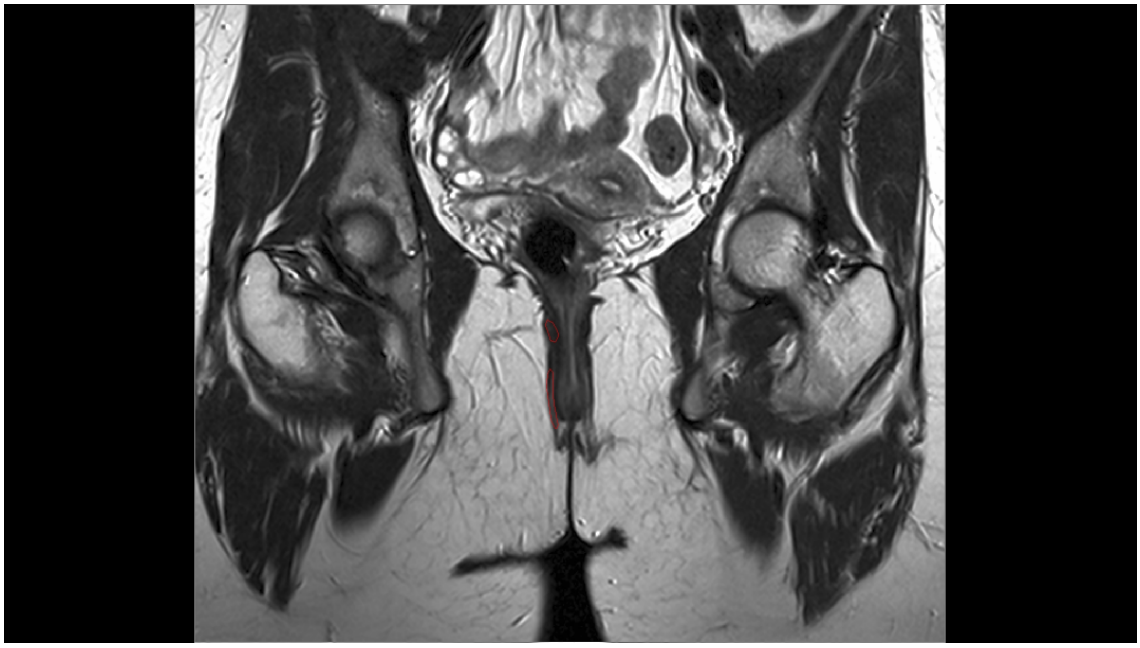
Quantitative assessment of atrophy of the EAS and PRM in all study participants was then carried out by one of the radiologists (observer ST) who again was blinded to the clinical details. Analysis was performed using the Jim analysis software package (version X, Xinapse Systems Ltd., Northants, UK, www.xinapse.com). Using an edge finding tool, the perimeter of the EAS (excluding the subcutaneous component) and PRM muscles on T2-weighted images were separately traced using the coronal or transverse slice where the largest bulk of muscle was visible. A fixed anatomical position was not used in this study due to variation in the nature of atrophy between individuals and therefore to prevent misrepresentation of the whole muscle. Only one side was marked as previous work has demonstrated the global nature of muscle atrophy in particular puborectalis muscle (Chatoor et al. 2009).

The T2 and VIBE images were spatially registered using an algorithm implemented in MATLAB (Guizar-Sicairos et al. 2008). Fat fraction maps were then produced from the fat and water images as described above in the validation protocol. The maps were converted to the NIFTI image format compatible with the JIM image analysis package.

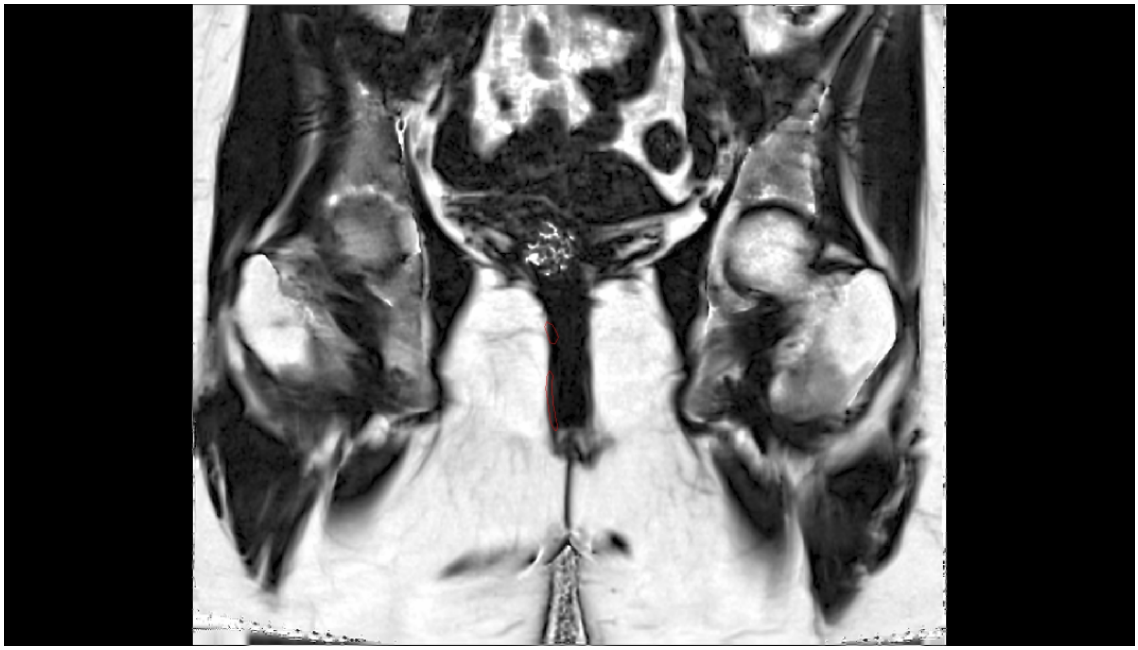
The regions of interest (EAS and PRM) outlined on the T2 weighted images were then transferred onto the corresponding fat fraction maps (figure 5.3). The area of the

outlined region of interest along with minimum, maximum and mean percentage fat values were then recorded by the principle researcher.

Figure 5.3 a) Coronal T2-weighted spin echo MR image of the anal sphincter complex with regions of interest (EAS and PRM) outlined.



b) Transfer of regions of interest onto corresponding fat fraction maps.



5.2.2.7 Statistical analysis

Statistical analyses were performed using SPSS version 19 (SPSS Inc., Chicago, IL, USA). Continuous data was tested for normality using the Kolmogorov-Smirnov test.

Summary statistics were reported as mean and standard deviation. Statistical significance of differences between the control and incontinent group for continuous variables were determined using the two sample t-test or Mann-Whitney U test where appropriate. For analysis purposes when the scans were repeated twice in controls the mean percentage fat values from the first set of scans were used.

Where repeated measurements of the mean percentage fat values of the EAS and PRM were made on the 10 controls that underwent repetition of the full scanning sequence, the Bland Altman limits of agreement method (Bland and Altman 1999) was used to assess for reproducibility.

The data for study subjects and controls were combined as one group for the remainder of the analysis. A one way analysis of variance (ANOVA) was performed to test for significant differences firstly between the objective mean percentage fat values of the EAS and PRM and subjective grade of atrophy on T2 MR images (as graded by ST) and secondly between the EAS mean percentage value and St Marks Incontinence Score severity subgroups. The Tukey honestly significant difference test for multiple comparisons was used for post hoc analysis. A chi squared test was used to look for a significant difference between the subjective grade of EAS atrophy as scored by radiologist ST on T2 MR images and St Marks Incontinence Score severity subgroups.

Spearman's rank correlation coefficient with a two tailed test of significance was used to determine a correlation between firstly, EAS and PRM mean percentage fat values and age, mean maximum incremental squeeze pressure and anal sensation; and secondly between grade of EAS and PRM atrophy and age and mean maximum incremental squeeze pressure.

Cohen's weighted kappa statistic with 95% CI was used to assess for interobserver agreement in the grading of EAS and PRM atrophy on the T2 weighted images.

A P-value of less than 0.05 was considered to be statistically significant in all analyses. The kappa values were interpreted as <0.20, poor agreement; 0.20-0.40, fair agreement; 0.41-0.60, moderate agreement; 0.61-0.80, good agreement; 0.81-1.00, very good agreement (Altman 1999).

5.3 Results

5.3.1 Validation of 2 point Dixon fat water decomposition MR imaging technique against MR spectroscopy in the quantification of muscle fat

There was good agreement between MR Spectroscopy and two point Dixon technique in the quantification of the fat fraction within gluteus maximus as demonstrated by the Bland Altman plot (figure 5.4) with a 95% limits of agreement of -6.0% to 3.9%. The mean fat fractions calculated by spectroscopy and two point Dixon technique were 15% and 16% respectively.

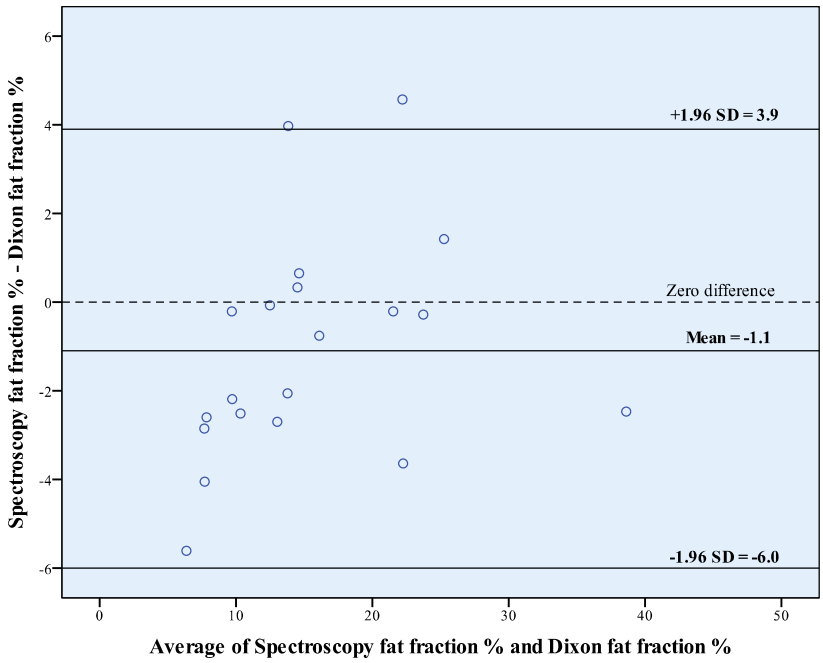


Figure 5.4 - Bland Altman plot assessing agreement between MR Spectroscopy and 2 point Dixon method in the measurement of fat fraction percentage.

5.3.2 Application of 2 point Dixon fat water decomposition MRI in the quantification of the anal sphincter complex in healthy controls and incontinent patients

5.3.2.1 Clinical Characteristics

Thirteen asymptomatic nulliparous controls (mean age 30 years, range 23-39 years) and nineteen faecally incontinent women, of which eight women also took part in chapter 4 (mean age 52 years, range 31-75 years, 9 primiparas, 10 multiparas) participated in this study. The median St Mark's Incontinence Score in the study group was 10 (range 3-17). The nature of faecal incontinence was urgency in 9 (47%), flatus incontinence in 9 (47%) and incontinence to solid and/or liquid stool in 12 women (63%). Based on the symptom severity 4 (21%) had mild (St Mark's Incontinence score <4), 2 (11%) had moderate (score 5-8) and 13 (68%) had severe (score >9) faecal incontinence.

Clinical and demographic characteristics of controls and study subjects are summarised in Table 5.1. The study group were significantly older and had a reduced squeeze pressure in comparison to the control group. No other apparent differences in physiological parameters or muscle fat content were found between the control and study group.

	Asymptomatic controls (n=13)	Faecally incontinent group (n=19)	p value
Age (yrs)	29.9 (5.2)	51.7 (19.3)	0.001
Mean squeeze pressure (cm H_20)	115.4 (48)	74.8 (38.7)	0.036
Anal sensation (mA)	9.6 (2.0)	10.3 (3.1)	0.506
Mean percentage EAS fat	21.3 (8.1)	27.9 (14.0)	0.11
Mean percentage PRM fat	10.6 (4.5)	13.1 (6.4)	0.328

Table 5.1 - Clinical and demographic characteristics of asymptomatic controls and faecally incontinent study subjects. Results are expressed as mean (SD). In the control group n=8 for mean squeeze pressure and anal sensation.

5.3.2.2 Subjective grading of EAS and PRM atrophy on MR Imaging

Controls

EAS atrophy was subjectively graded as 1 (no thinning or no replacement of muscle by fat) in 6 controls and 2 (<50% thinning or replacement of muscle by fat) in 7 controls. No controls had evidence of grade 3 (>50% thinning or replacement of muscle by fat) EAS atrophy. A majority of the asymptomatic controls (n=10) were found to have no evidence of PRM atrophy (grade 1) on T2 weighted MR imaging; however 3 controls were reported to have grade 2 atrophy of the PRM.

Study subjects

EAS atrophy was graded as 1 in 7 subjects, 2 in 7 subjects and 3 in 5 subjects. PRM atrophy was reported to be present in 7 study subjects and subjectively graded as 1 in 12 subjects, 2 in 4 subjects and 3 in 3 subjects.

5.3.2.3 Comparison between subjective EAS and PRM atrophy scores on T2 weighted MR imaging and objective mean percentage fat content using two point Dixon MRI technique

The results of the comparison between subjective grading of EAS and PRM atrophy on T2 weighted MR imaging and the corresponding mean percentage fat data of all 32 subjects are displayed in table 5.2 and figures 5.5 and 5.6.

The overall mean percentage fat content of the EAS was 19.8% for grade 1 atrophy, 26.4% for grade 2 atrophy and 36% for grade 3 atrophy (ANOVA p=0.03). A Tukey post-hoc analysis revealed a significant difference in mean percentage fat content between grade 1 and grade 3 EAS atrophy (p=0.027). No significant difference between grade 1 and 2 EAS atrophy (p=0.29) and grade 2 and 3 EAS atrophy (p=0.25) was found.

The overall mean percentage fat content was 11 % in grade 1 PRM atrophy, 13% in grade 2 PRM atrophy and 17% in grade 3 PRM atrophy. No statistical significant difference in mean percentage fat content of the PRM was demonstrated between the 3 gradings (p=0.21).

Subjective Grade of Muscle Atrophy	Number of subjects	Overall mean percentage fat content	95% CI (%)
EAS			
1	13	19.8 (14.2)	11.3 - 28.4
2	14	26.4 (8.6)	21.5 - 31.4
3	5	36 (8.4)	25.6 - 46.5
PRM			
1	22	11 (5.5)	8.6 - 13.5
2	7	13.2 (4.3)	9.2 - 17.2
3	3	17.1 (9.5)	-6.6 - 40.7

Table 5.2 Comparison between subjective grade of EAS and PRM atrophy on T2 weighted MR imaging and mean percentage fat content of the EAS and PRM with two point Dixon MRI technique. Data in brackets represents standard deviation.

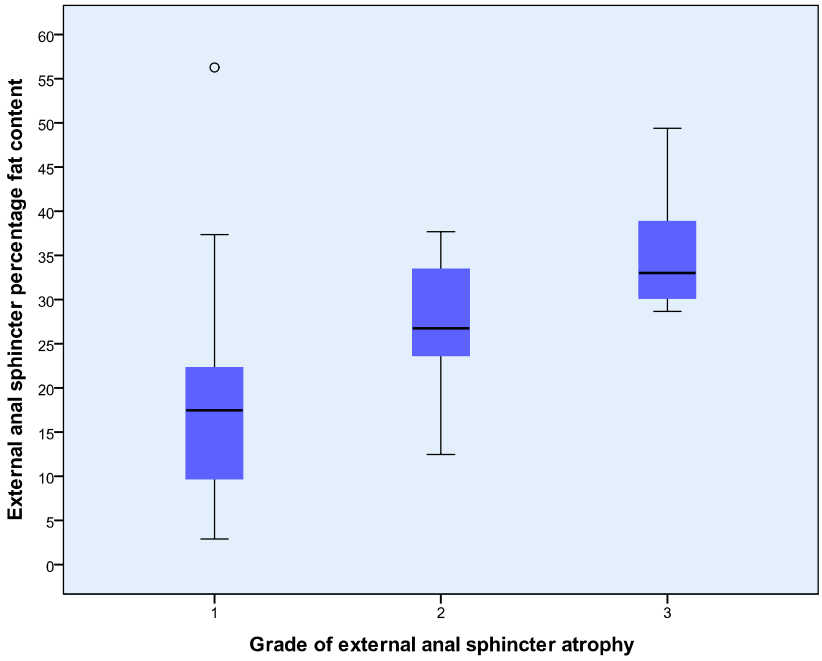


Figure 5.5 Box plot demonstrating appearance of the EAS on T2 weighted MR images with the mean percentage fat content of the EAS calculated with the two point Dixon MR technique in all 32 subjects. The upper and lower limits of the box represent the 25th and 75th percentiles, the line within the box represents the 50th percentile (median) and the lines outside the box represent the minimum and maximum values (with exception to grade 1 which has 1 outlier).

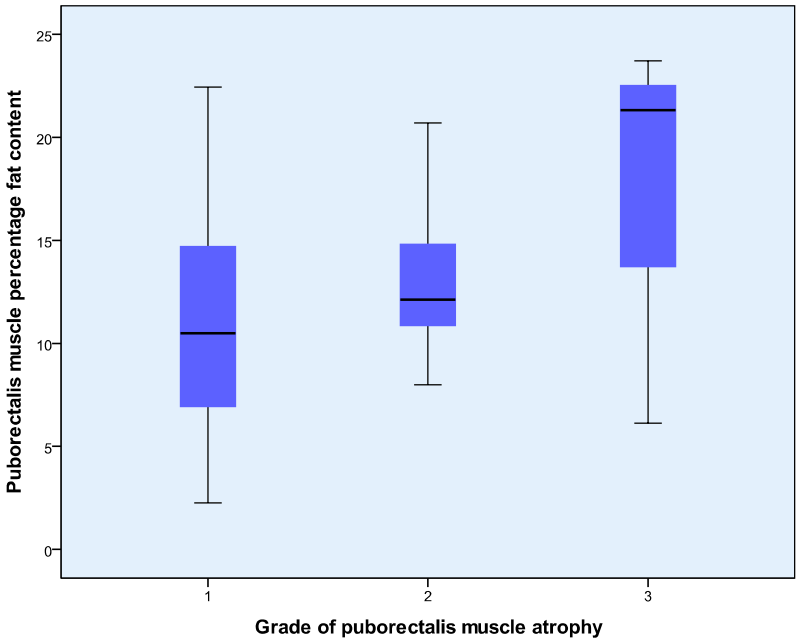


Figure 5.6 Box plot demonstrating appearance of the PRM on T2 weighted MR images with the mean percentage fat content of the PRM calculated with the two point Dixon MR technique in all 32 subjects. The upper and lower limits of the box represent the 25th and 75th percentiles, the line within the box represents the 50th percentile (median) and the lines outside the box represent the minimum and maximum values.

5.3.2.4 Comparison between symptom scores and mean percentage fat content of the external anal sphincter using two point Dixon MRI technique

The overall mean percentage fat content of the EAS was 20% in those with mild incontinence symptoms, 28% in the moderate and 32% in the severe SMIS subgroup (figure 5.7) (ANOVA p=0.03). A Tukey post-hoc analysis revealed a significant difference in mean percentage fat content between the mild and severe symptom subgroups (p=0.024). No significant difference between the mild and moderate SMIS subgroups (p=0.61) and moderate and severe subgroups (p=0.91) were found. In contrast, no significant difference was found between the subjective grade of EAS atrophy and SMIS subgroup (p=0.07).

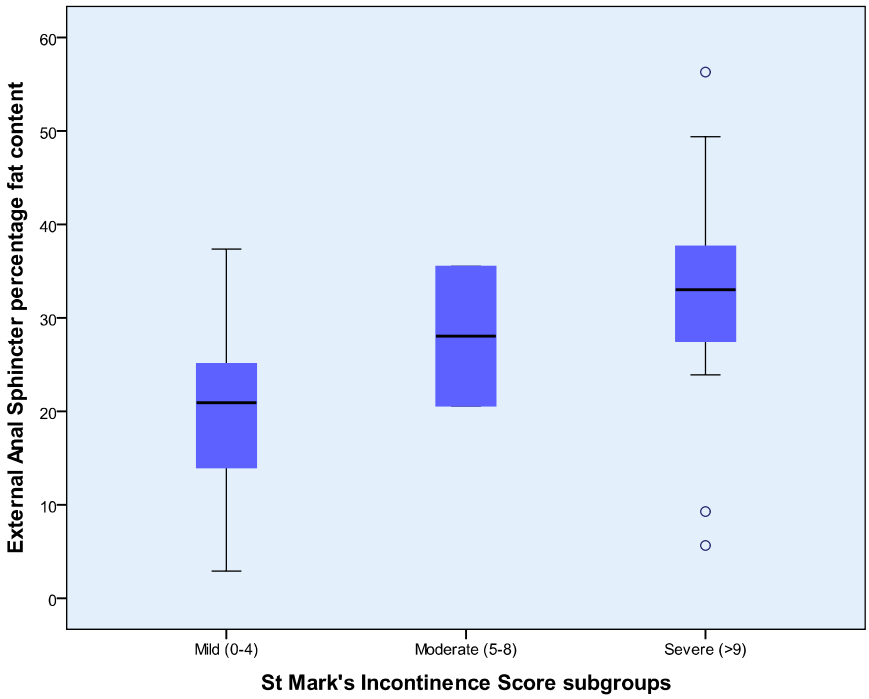


Figure 5.7 Box plot demonstrating the St Mark's Incontinence Score subgroup with the mean percentage fat content of the EAS calculated with the two point Dixon MR technique in all 32 subjects. The upper and lower limits of the box represent the 25th and 75th percentiles, the line within the box represents the 50th percentile (median) and the lines outside the box represent the minimum and maximum values (with exception to the severe subgroup which has 3 outliers).

5.3.2.5 Correlations

The subject age was found to correlate with subjective grade of EAS ($p<0.01$, $r=0.59$) and PRM ($p<0.01$, $r=0.62$) atrophy. A significant correlation was also found between subject age and mean percentage fat content of the EAS ($p=0.001$, $r=0.57$) but not with mean percentage fat content of the PRM ($p=0.23$). There was a trend for more atrophied muscles to have a poor squeeze pressure however the correlation failed to reach statistical significance ($p=0.09$ for EAS and $p=0.08$ for combined EAS and PRM percentage fat content). No correlation between the grade of EAS atrophy ($p=0.38$) or the mean percentage PRM fat content ($p=0.82$) with mean maximal squeeze pressure was found. Anal mucosal electrical sensitivity was found to correlate with mean maximal squeeze pressure ($p=0.02$) but failed to correlate with the mean percentage fat content of EAS ($p=0.43$) or age ($p=0.25$).

5.3.2.6 Interobserver agreement in grading of EAS and PRM atrophy on T2 weighted MR imaging

There was poor interobserver agreement in the grading of EAS atrophy (k=0.19, 95% CI -0.04-0.42) with both observers agreeing in 14 of 32 patients (44%).

Agreement between observers in the grading of atrophy of the PRM was only minimally better (k=0.23, 95% CI 0.02-0.44) with both observers agreeing in 16 of 32 patients.

5.3.2.7 Reproducibility

Where measurements of mean percentage fat values of the EAS and PRM were repeated on 10 controls, the mean of the differences of the EAS mean percentage fat measurement between the two readings was -3% with a 95% confidence interval of -28.6 to 22.6% and standard deviation of 13.05% (figure 5.8).

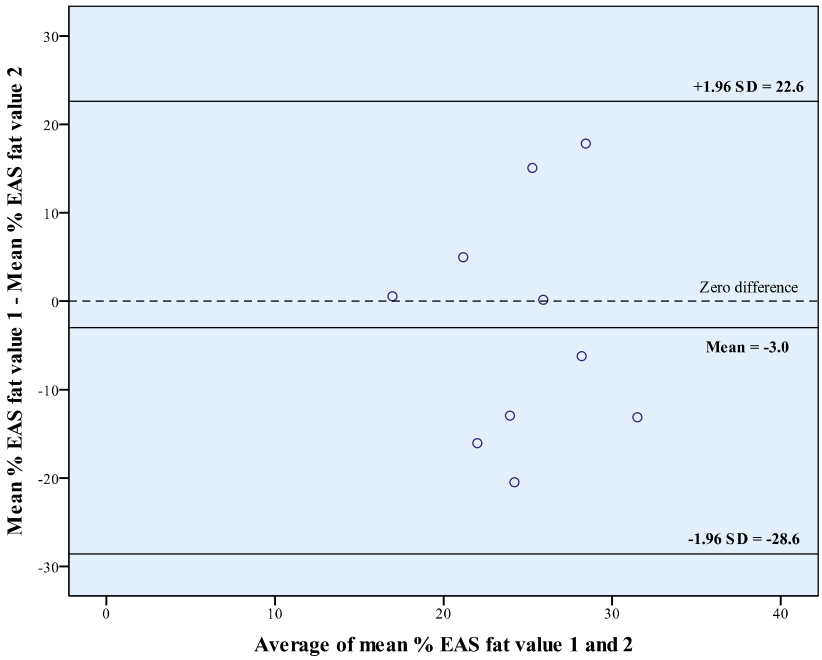


Figure 5.8 - Bland Altman plot showing differences between the mean percentage EAS fat value versus the average of the mean percentage EAS fat value with 95% limits of agreement in 10 pairs of repeated measurements.

The differences between the two PRM mean percentage fat measurements had a mean of -2.2% with a 95% confidence interval of -22.4 to 18% and a standard deviation of 10.3% (figure 5.9).

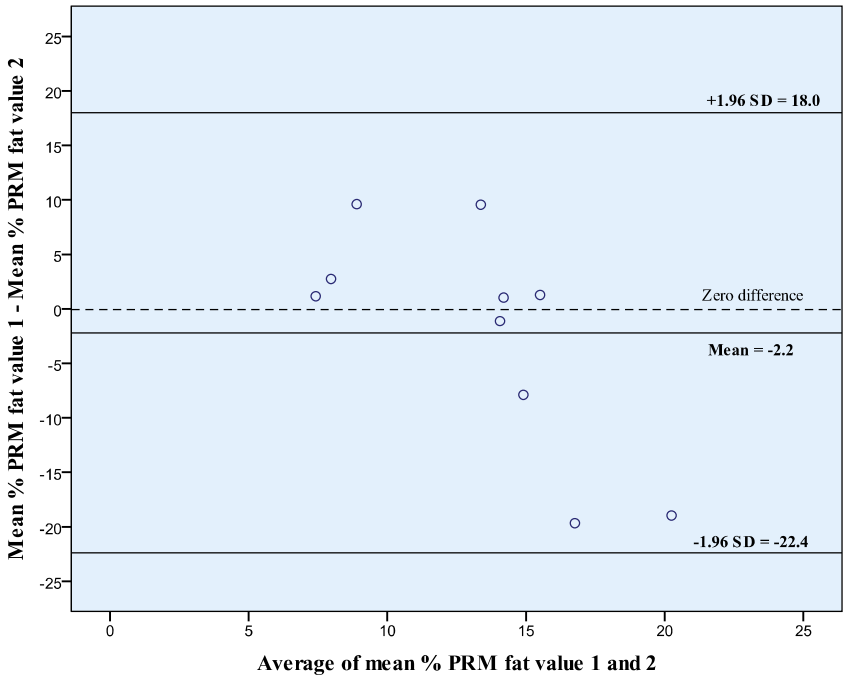


Figure 5.9 - Bland Altman plot showing differences between the mean percentage PRM fat value versus the average of the mean percentage PRM fat value with 95% limits of agreement in 10 pairs of repeated measurements.

Although all 10 measurements for both the EAS and PRM lie within 95% limits of agreement as demonstrated in figures x and y, the difference in mean percentage EAS and PRM fat values between the two repeated measurements (-28.6 to 22.6% and -22.4 to 18% respectively) are too large to be acceptable in clinical practice suggesting a poorly reproducible method.

5.4 Discussion

External anal sphincter atrophy is considered to be the result of denervation injury and is characterised by extreme thinning of muscle fibres often associated with generalised fatty infiltration (Briel et al. 2000). Detection of atrophy of either the external anal sphincter and/or puborectalis muscles in faecally incontinent patients plays an important role in the prognosis of surgical treatment. For example, it has been shown that external anal sphincter atrophy secondary to obstetric anal sphincter injury and pelvic floor denervation is associated with poor symptomatic outcome following surgery (Briel et al. 1999). As yet no universal criteria for the diagnosis of atrophy has been established with imaging modalities such as endoanal and external phased-array MRI. A subjective assessment by the reporting radiologist is the norm in current clinical practice. MR

spectroscopy is an emerging technique to quantify fat in large skeletal muscles and organs (Boesch et al. 1997, Schick et al. 1993; Szczepaniak et al. 1999, Kreis et al. 1996; Schick et al. 2002). However, its use in evaluating such fatty atrophy of the pelvic floor and anal sphincter complex may be potentially limited due to the small size of these structures and contamination of fat fraction values by extra-voxel fat. Further limitations on the use of MR spectroscopy are the long scan time and need for a skilled operator to carry out the imaging, process the data and interpret the results hence restricting its use in everyday clinical practice (Lee et al. 2010). Unlike MR spectroscopy, the 2 point Dixon MRI has a shorter scanning time, is easier to perform and can be easily added to routine MR protocols.

Before using the two point Dixon method to quantify EAS and PRM fat content I carried out a comparative study to validate this technique against the gold standard MR spectroscopy in the larger adjacent gluteus maximus muscle. My validation study showed a good agreement between the two methods, therefore allowing myself to define the utility of the two point Dixon method in quantifying muscle fat content in subjects with and without faecal incontinence. To my knowledge this is the first study to use the two point Dixon technique to quantify fat content of the PRM and EAS along with relating sphincter morphology to function.

Objective measurement of the fat content of the EAS has been reported to be useful in diagnosing atrophy of the EAS (Terra et al. 2006, Briel et al. 1999, Williams et al. 2001, Briel et al. 2000). I found the mean percentage fat content quantified by the Dixon method to be significantly lower in patients with subjectively graded EAS atrophy score of 1 compared to patients with grade 3 atrophy although I found no such relationship for the PRM. Several previous studies have reported no relationship between symptoms and muscle structure (Voyvodic et al. 2003, Terra et al. 2006). In contradistinction I found firstly, a significant difference in the mean percentage fat content of the EAS between those with mild, moderate and severe St Marks Incontinence score subgroups and secondly, no significant difference between the subjective grade of EAS atrophy and St Marks Incontinence Score subgroup indicating that the 2 point Dixon method was better than the subjective atrophy score in dividing the three symptom severity groups. One must be cautious when comparing studies due to the lack of consistency in validated symptoms score questionnaires used, variation in the definition and subgrouping of the

severity of symptoms and different radiological imaging techniques used to assess structure of the anal sphincter complex.

In healthy continent subjects, aging has been shown to result in progressive thinning of the EAS although this change remains to be quantified (Haas and Fox 1990; Rociu et al. 2000; Williams et al. 2001). In this study, a strong correlation between age and fat content of the EAS and subjective grade of EAS and PRM atrophy was demonstrated. Interestingly, no association between maximum squeeze pressure and grade of EAS or PRM atrophy or fat content of the EAS or PRM was found, although there was a trend for more atrophied muscles to have a lower squeeze pressure. This association is likely to be a type II error due to the small sample size used in this study. Very few studies have quantified fatty atrophy of the anal sphincter complex on MR imaging and looked at the relationship between atrophy and function in patients with faecal incontinence. Williams et al. 2001 were the first to look at the relationship between quantitative parameters of sphincter anatomy on endocoil MRI and function in faecally incontinent patients with intact anal sphincters. They demonstrated a correlation between squeeze pressure, cross sectional area and percentage fat content of the EAS but failed to show a relationship between EAS thickness and cross sectional area. The difference in outcomes in my study could be explained by a number of factors; firstly, the patient cohort studied, Williams et al included only symptomatic women with intact sphincters where as I included symptomatic women with sphincter defects; secondly, the region of interest, Williams et al. 2001 used a fixed anatomical position to measure the width and percentage fat content of the sphincter where as I used the slice where the largest bulk of muscle was visible; thirdly, the method used to quantify the fat content within the muscle, I used the two point Dixon fat water decomposition technique which was validated against the current gold standard MR spectroscopy whereas Williams et al. 2001 looked at the pixel density within the region of interest to quantify the fat content. Finally the grading systems used to classify atrophy were different.

The relatively high degree of intra-subject variability seen in the measurement of the mean percentage fat content of both muscles suggests reproducibility of this method may be sub-optimal. Such variations in values may be accounted for by the lack of fixed size and positioning of the region of interest hence indicating the need for a more objective way of defining the region of interest. Although reproducibility could be

improved by using a fixed ROI size and fixed anatomical positioning, clearly this would run the risk of underestimating atrophy, particularly in cases of patchy or asymmetrical atrophy. Chatoor et al. 2009 reported a high correlation between the objective lipid content of the right and left puborectalis muscle using MR spectroscopy suggesting atrophy to be a global process and therefore in theory it should not matter on which side the region of interest is placed within the muscle. However it is possible that fat infiltration of the pelvic floor musculature and anal sphincter complex may occur focally around a point of traumatic injury indicating the need for further studies sampling multiple regions of interest for a more accurate representation of the sphincter quality.

As yet no fixed criteria for the visual diagnosis of EAS or PRM atrophy on MRI have been established (Terra et al. 2006). Studies have shown a large variation in the ability to depict atrophy of the EAS on pelvic floor MR images amongst radiologists of varying experience (Terra et al. 2005; Terra et al. 2006). My study found poor inter-observer agreement for the grading of EAS atrophy and fair agreement for the grading of PRM atrophy which is in keeping with previous data (Terra et al. 2006; Terra et al. 2005). This observation is not surprising given the subjective, simplistic grading system used for atrophy in this study and may explain the presence of muscle atrophy in some of the controls. However as noted above, age is associated with fatty infiltration and not all controls were below 30 years. Although ideally data comparing MRI and histology would be very useful to validate either objective or quantitative methods of assessing fatty atrophy, such data is very difficult to collate.

There were a number of limitations in my study. Firstly, the number of subjects examined was relatively small thus limiting the power of the study. Secondly, compared to the control group, the symptomatic study group were significantly older and more heterogeneous in their makeup with the inclusion of idiopathic and obstetric trauma related incontinent subjects which may have affected the results of this study. In particular the study group consisted of 8 incontinent women with an acute obstetric anal sphincter tear and hence the length of follow up (median 10 months range 7-15 months) may have been too early to see atrophic muscle changes on MR imaging. The remainder of the study group had endoanal ultrasonography reporting the presence of external anal sphincter and/or puborectalis muscle atrophy prior to inclusion in the study. Thirdly, I

did not use histology as a reference standard to confirm muscle atrophy because not all subjects would have been suitable for secondary sphincter repair as atrophy is known to be a poor prognostic factor for surgical repair. Finally, I was able to demonstrate excellent agreement between the gold standard MR spectroscopy and the 2 point Dixon technique in the quantification of fat in the skeletal muscle gluteus maximus.

CHAPTER SIX

SUMMARY AND CONCLUSION

6.1 Introduction

The pelvic floor is a complex structure composed of the endopelvic fascia, pelvic diaphragm (or levator ani muscle), urogenital diaphragm and superficial transverse perineii muscles and is traversed by the vagina, anal and urethral sphincter muscles. Together the pelvic floor musculature act as one functional unit preserving continence and providing structural support to the pelvic organs. More specifically, the puborectalis-pubococcygeus complex or pubovisceral muscle component of the levator ani muscle forms a v-shaped sling around the anorectal junction, inserting into the pubic bone anteriorly. Voluntary contraction of the medial puborectalis causes closure of the anal canal or decrease in the anorectal angle thus enhancing the faecal continence mechanism.

Pelvic floor dysfunction encompassing pelvic organ prolapse, urinary and faecal incontinence is an important women's health issue. Vaginal delivery causes acute distension of the levator ani muscle potentially resulting in stretching, avulsion or neurologic injury and is thought to be a key factor in the multifactorial aetiology of subsequent atrophy and dysfunction of the pelvic floor complex. However, although levator ani injury is associated with pelvic organ prolapse a clear correlation with faecal incontinence remains to be established. This may occur because patients with a traumatised puborectalis maintain continence through preserved distal anal sphincter function, compensating for the loss of the proximal component.

Atrophy of the pelvic floor complex secondary to obstetric trauma, neurogenic injury and ageing is firstly thought to play an important role in the development of incontinence and pelvic organ prolapse and secondly, may explain the poor prognostic outcome following surgical repair. Structural evaluation of pelvic floor atrophy has been carried out using endoanal MRI and external phased array MRI however this only allows semi-quantitative assessment of fatty atrophy.

Up until the present there has been difficulty in understanding the role of puborectalis function due to the absence of a standardised measurement technique. So far, MRI has been proposed for accurate structural assessment however, no consensus has yet been reached on the 'gold standard' for the physiological measurement of puborectalis strength. It is also important to appreciate the different entities involved in evaluating

puborectalis function (i.e. the ability to contract) and strength (i.e. the ability to squeeze). Due to the close proximity of the puborectalis and external anal sphincter, it remains to be seen how current physiological measures can accurately discriminate between the two structures. Clinically an accurate assessment of puborectalis function is to provide a baseline evaluation and response to treatment of puborectalis muscle strength and will help to determine the role of puborectalis in maintaining faecal continence in the presence of a defective anal sphincter complex.

This thesis firstly aimed to identify risk factors associated with obstetric anal sphincter injury with subsequent evaluation of anorectal symptoms, anal sphincter structure and function and secondly looked at novel structural and physiological measures in the assessment of pelvic floor function and atrophy. The cohort of study participants selected included healthy nulliparous controls, women presenting to the Birth Injuries Clinic with clinically reported third or fourth degree anal sphincter tears and women presenting to the GI Physiology unit with chronic idiopathic or obstetric trauma related faecal incontinence.

6.2 Risk factors and outcomes of obstetric anal sphincter tears

The risk factors associated with obstetric anal sphincter disruption and subsequent development of impaired faecal continence were discussed in chapter 3.The data for my prospective observational study was collated from a well established computerised maternity database therefore ensuring the data was robust and that births were recorded in a time consecutive and standardised manner with minimal missing data sets. My study identified the following:

- Similar risk factors for obstetric anal sphincter injury were identified in my study in comparison to previous American and European studies.
- Multivariate analysis confirmed the non modifiable variables nulliparity (OR 3.2) and foetal birthweight greater than 4kg (OR 2.05) and the modifiable variable instrumental assisted delivery (OR 3.13) as independent risk factors in the development of anal sphincter tears.

- No association between the incidence of faecal incontinence symptoms and clinically or sonographically detected anal sphincter defects or scarring.
- No association between anorectal physiological function and symptoms was identified in this study, implicating pathology beyond the anal sphincter.
- Maternal age (OR 1.1) was the single risk factor associated with faecal incontinence following an anal sphincter tear.
- There was a trend for the symptomatic women with clinically identified anal sphincter tears to have lower anal sensation, rectal capacity and mean resting and squeeze pressures in comparison to the asymptomatic group with the same pathology. This may, speculatively, indicate the presence of pudendal neuropathy in addition to traumatic sphincter injury in this group.

Limitations of this study included

- Due to the lack of availability of an accurate physiological test to quantify pudendal nerve function I was unable to comment on the neurological contribution to alterations seen in anorectal function and symptoms between the symptomatic and asymptomatic obstetric tear groups.
- The lack of a group of matched controls without anal sphincter tears in this study means I was unable to compare the changes in anorectal function, incidence of occult tears and incontinence symptoms following childbirth with such control subjects.
- Longer term follow up was required in the symptomatic women with obstetric anal sphincter tears, with inclusion of women with subsequent deliveries.
- The obstetric data I collected was limited to the current birth and the details entered into the clinical database utilised by the obstetric department. Therefore I was unable to look at factors which may have influenced the risk of sphincter injury such as antepartum bowel symptoms, maternal ethnicity, birth delivery position and level of experience of obstetricians performing instrumental deliveries and repairing the anal sphincter tears.

6.3 Vaginal manometry in the assessment of pelvic floor strength

Various physiological methods have been proposed for the measurement of pelvic floor strength as discussed in chapter 1. The most promising technique so far is that reported by Guaderrama et al. 2005 who demonstrated the presence of a vaginal high pressure zone reflective of pelvic floor contraction with the use of water perfused vaginal manometry. My study attempted to identify the vaginal pressure profile during rest and voluntary contraction of the pelvic floor in asymptomatic nulliparous female controls and faecally incontinent women presenting to the Birth Injuries Clinic with a clinically diagnosed anal sphincter tear. I was able to report the following:

- The most important finding was a negative one; It was not possible to identify the previously described vaginal high pressure zone with the use of vaginal manometry in either nulliparous controls or symptomatic women. Although the catheter design used in my study was slightly different to that used by Guaderrama et al. 2005 both systems used were water perfused hence measuring precise absolute pressure. One can conclude that either the vaginal high pressure zone does not actually exist or my results may be due to a type II error, however this is highly unlikely as both studies were done on the same number of control patients.
- Although greater squeeze pressures were generated along the whole length of the vaginal canal during pelvic floor contraction in controls compared to study subjects no consistent pattern was observed in either group.
- Cough resulted in the consistent generation of an identical pressure wave along the full length of the vaginal canal in all controls and study subjects. I speculate that cough is a measure of pelvic floor closure and contraction and not a measure of intra-abdominal pressure as previously thought.
- There was poor agreement between vaginal and anorectal manometry in the measurement of pelvic floor squeeze. Whilst it has been shown that vaginal manometry can potentially quantify pelvic floor squeeze there is a lack of understanding regarding which muscle and what proportion of individual muscles of the pelvic floor contribute to the genesis of the vaginal squeeze pressure. In comparison anorectal manometry has been shown to measure only

puborectalis muscle squeeze in the proximal anal canal. Therefore these two methods may not be measuring pressures generated by the same structure and hence cannot be compared.

Limitations and confounders to this study included

- Due to the nature of the referrals from the birth injury clinic selected study participants were first assessed manometrically based upon a clinical diagnosis of obstetric anal sphincter injury and the presence of symptoms of faecal incontinence. Therefore subjects later confirmed by endoanal ultrasonography with an intact anal sphincter may have been symptomatic as a result of pudendal nerve injury.
- The cause of the symptoms in the study group could have been a result of pure anal sphincter injury, pelvic floor muscle avulsion or rupture and pudendal neuropathy or a combination of these three. However, as I was not able to determine the presence of denervation injury due to the lack of availability of a reliable test to measure pudendal nerve function it would not have been practically possible to subdivide the already small number of subjects in this group to different pathologies.
- I did not exclude breastfeeding subjects from the study as this would have largely reduced the number of participants eligible for the study from my cohort.

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6.4 A novel quantification of pelvic floor atrophy: validation of technique and its utility in faecal incontinence

Imaging modalities currently used to identify atrophy of the anal sphincter complex and pelvic floor musculature were reviewed in chapter 2. Proton MR spectroscopy has been used to non-invasively quantify lipid content of muscle tissue however its use in smaller muscles such as the EAS is limited due to contamination by extra-voxel fat. My study looked at an alternative form of MR imaging known as the two point Dixon fat water decomposition method to accurately quantify EAS and PRM atrophy. I initially validated the two point Dixon fat-water decomposition method against MR spectroscopy in the measurement of gluteus maximus fat fraction and subsequently used

this technique to quantify atrophy of the EAS and PRM in healthy controls and faecally incontinent subjects. My results showed:

- The assessment of fat content of the EAS and PRM is feasible with the 2 point Dixon fat water decomposition method and presents a promising objective measure of fatty atrophy of the sphincter and pelvic floor complex.
- The fat content in subjects qualitatively scored as having good EAS quality i.e. grade 1 atrophy, was significantly lower than subjects scored as having poor EAS quality i.e. grade 3 atrophy. No such relationship was found for the PRM.
- There was a significant relationship between quantified EAS fat content and symptom severity subgroup and not between subjective EAS atrophy score and symptom severity subgroup, which is different to findings from previous studies. My results suggest that the 2 point Dixon method may be better than the subjective atrophy score in dividing the three symptom severity groups.
- A strong correlation between age and fat content of the EAS and subjective grade of EAS and PRM atrophy was demonstrated.
- There was a trend for more atrophied muscles to have a lower squeeze pressure however this failed to reach statistical significance. This may represent a type II error.

Limitations of this study included

- The patient cohort was small as a result of the short time period I had to recruit eligible candidates for the study, along with the claustrophobic nature of the MRI scanning machine which deterred willing study participants, therefore limiting the power of the study.
- The heterogenous make up of the study group was once again limited by time constraints and the number of study participants.
- The lack of use of histology of EAS and PRM as a gold standard to confirm atrophy.
- Histology of the EAS and PRM was not used as a gold standard to confirm atrophy in this study because not all subjects would have been suitable for secondary sphincter repair.

6.5 Future Directions

- Repetition of the chapter 3 study measuring the vaginal pressure profile in asymptomatic controls and pathological patients using the same catheter design utilised by Guaderrama et al. 2005 to determine any differences in the vaginal pressures recorded.
- The development of a more sensitive test to quantify pudendal nerve function is required to allow us to assess the degree of pudendal nerve damage and its subsequent contribution to symptoms and changes in anorectal manometry particularly in primiparous and multiparous women.
- Poor results of primary sphincter repairs identified sonographically warrant further studies to improve the training of obstetricians performing the primary repair along with exploring other treatment strategies such as delayed primary surgical repair of tears, earlier performance of endoanal ultrasonography to identify defects and involvement of colorectal surgeons from the outset in primary sphincter repair.
- The development of alternative physiological methods in quantifying pelvic floor function are required potentially providing complimentary information to that obtained with MR imaging.
- A study involving examination under anaesthesia of the anus with biopsy of the EAS in a cohort of healthy controls, women with idiopathic and chronic obstetric trauma related faecal incontinence would provide histology which could be used as a gold reference standard to validate a visual grading system for EAS atrophy on MRI.
- Future studies to establish the percentage fat content cut off points quantified by the Dixon method for the corresponding grades of muscle atrophy are required with possible use of histology as the gold reference standard.
- The clinical application of the Dixon MRI method in quantifying sphincter atrophy in the selection for surgical sphincter repair needs further exploration.
- Increased number of symptomatic study participants with further subdivision within this group to determine the influence of firstly, parity and secondly, time between initial insult to the pelvic floor and symptomatic presentation of sphincter atrophy is required.

- The poor reproducibility of the EAS and PRM fat content measured within the region of interest could be improved by calculating a mean value over 3 consecutive MR slices in the axial plane, therefore providing a more accurate representation of sphincter quality.
- Further studies exploring the utility and feasibility of producing better quality, higher resolution T2 MR images and Dixon scans therefore allowing more accurate identification of muscle structures by radiologists along with providing a more accurate and reproducible region of interest.
- Many studies have shown poor prognostic outcome of EAS atrophy with surgical sphincter repair. More recently, alternative therapies such as percutaneous tibial nerve stimulation therapy (PTNS) have been established and report encouraging results in patients with faecal incontinence secondary to EAS atrophy. There may be a role for Dixon MR imaging in looking at the anal sphincter muscle structure at baseline and the changes following PTNS along with identifying anatomical differences depicted on MRI between subjects with successful or failed response.

CHAPTER SEVEN

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CHAPTER EIGHT

APPENDICES

8.1 Appendix 1

Biofeedback Services at University College Hospital Gastrointestinal Physiology Unit

The biofeedback therapy service forms an essential component of the GI physiology unit at UCLH. It is a mature established service which has been operational for 6 years and is run by 2 specialist nurses. In the context of this study, all symptomatic women with clinically reported obstetric anal sphincter injuries, missed tears confirmed on ultrasound or over reported degree of anal sphincter tears i.e. intact anal sphincter on endoanal ultrasound are routinely referred for therapy following completion of anorectal manometry.

A thorough clinical history is taken by the specialist nurse on the first appointment focussing mainly on bowel habits pre partum along with changes which have occurred since their delivery followed by assessment of evacuation technique using a balloon mounted on a catheter. Therapy involves education regarding function of the anal sphincter mechanism and exercises to strengthen and improve endurance and coordination of the anal sphincter muscles. Advice about standard bowel care, diet, posture whilst sitting on the toilet and brace technique for evacuation are also discussed.

Patients are typically seen for two 1 hour appointments 4-6 weeks apart with a final review either face to face or over the telephone at 3 months following their first appointment. Patients are either discharged from biofeedback if there has been a good response to the therapy or are referred on for more invasive treatments offered within the unit. All patients are able to directly contact the specialist nurses for support outside of these fixed appointments by telephone if necessary.)

8.2 Appendix 2

St Mark's Incontinence Score symptom questionnaire

	Never	Rarely	Sometimes	Weekly	Daily
Incontinence for solid stool	0	1	2	3	4
Incontinence for liquid stool	0	1	2	3	4
Incontinence for gas	0	1	2	3	4
Alteration in lifestyle	0	1	2	3	4
				No	Yes
Need to wear pad / plug				0	2
Taking constipating medicines				0	2
Lack of ability to defer defecation for 15 minutes				0	2

Never = no episodes in the past four weeks

Rarely = 1 episode in the past 4 weeks

Sometimes =>1 episode in the past 4 weeks but <1 per week

Weekly = 1 or more episode a week but <1 per day

Daily = 1 or more episodes a day

Minimum score = 0 perfect continence

Maximum score = 24 totally incontenent

8.3 Appendix 3

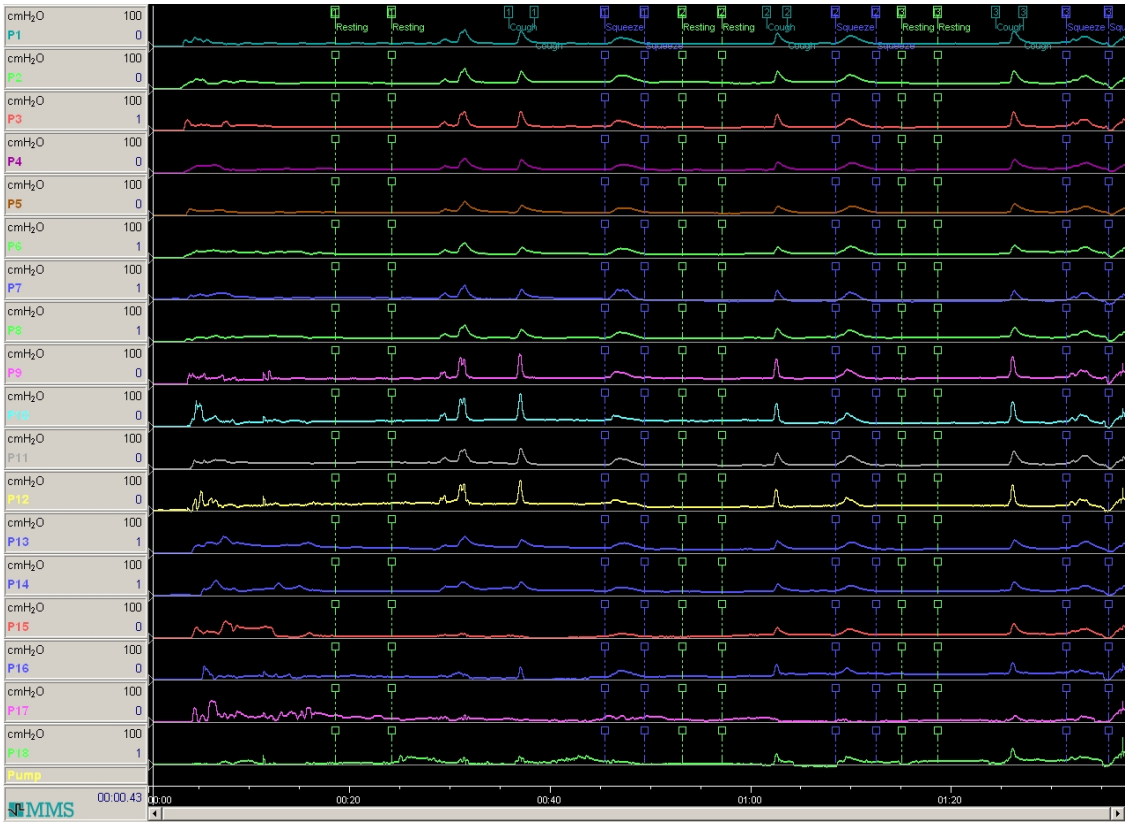
Breakdown of Study Cohort to Demonstrate Overlap of Subjects Used in Each Study

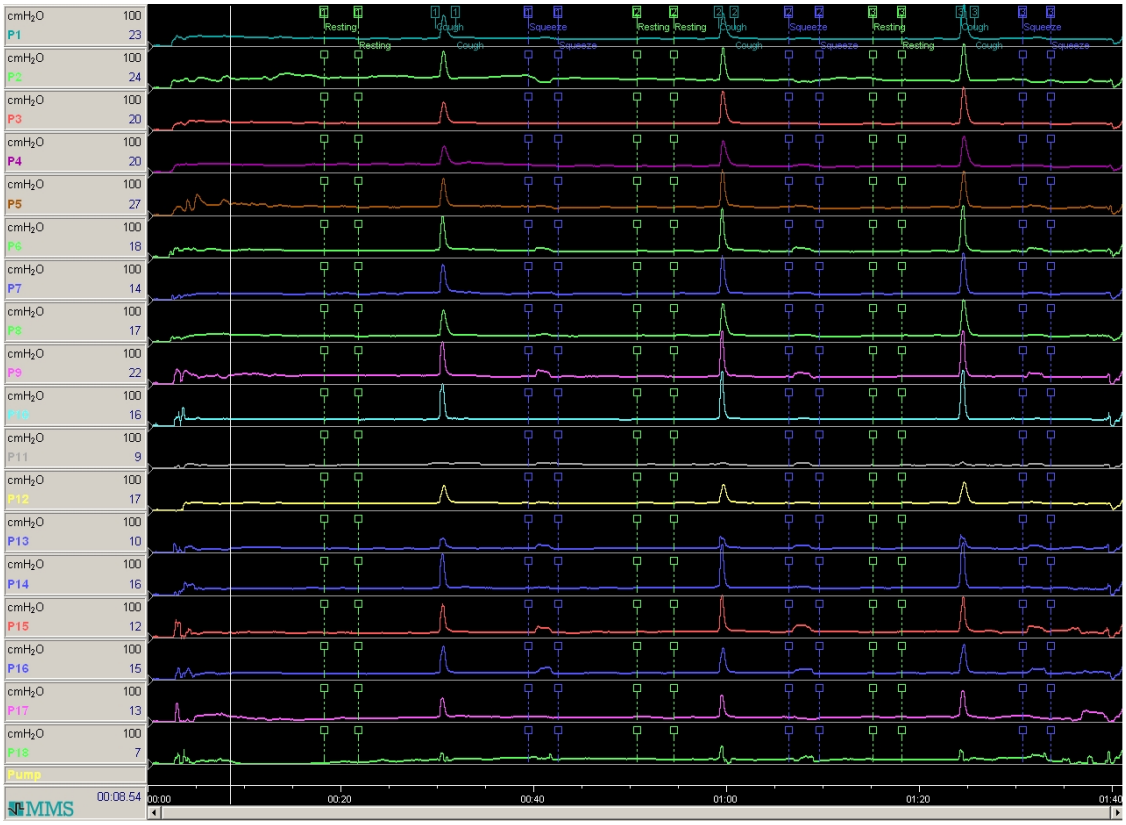
Study Group	Vaginal Manometry	MRI
Number of Patients		
8 (Birth Injuries Clinic)	Yes	Yes
36 (Birth Injuries Clinic)	Yes	No
11 (GI Physiology Clinic)	No	Yes
Number of Controls		
4	No	Yes
5	Yes	No
9	Yes	Yes

8.4 Appendix 4

Example vaginal manometry traces

8.4.1 Vaginal manometry traces from symptomatic patients during rest, cough and squeeze repeated 3 times.

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P5 27
P6 18
P7 14
P8 17
P9 22
P10 16
P11 9
P12 17
P13 10
P14 16
P15 12
P16 15
P17 13
P18 7
Pump
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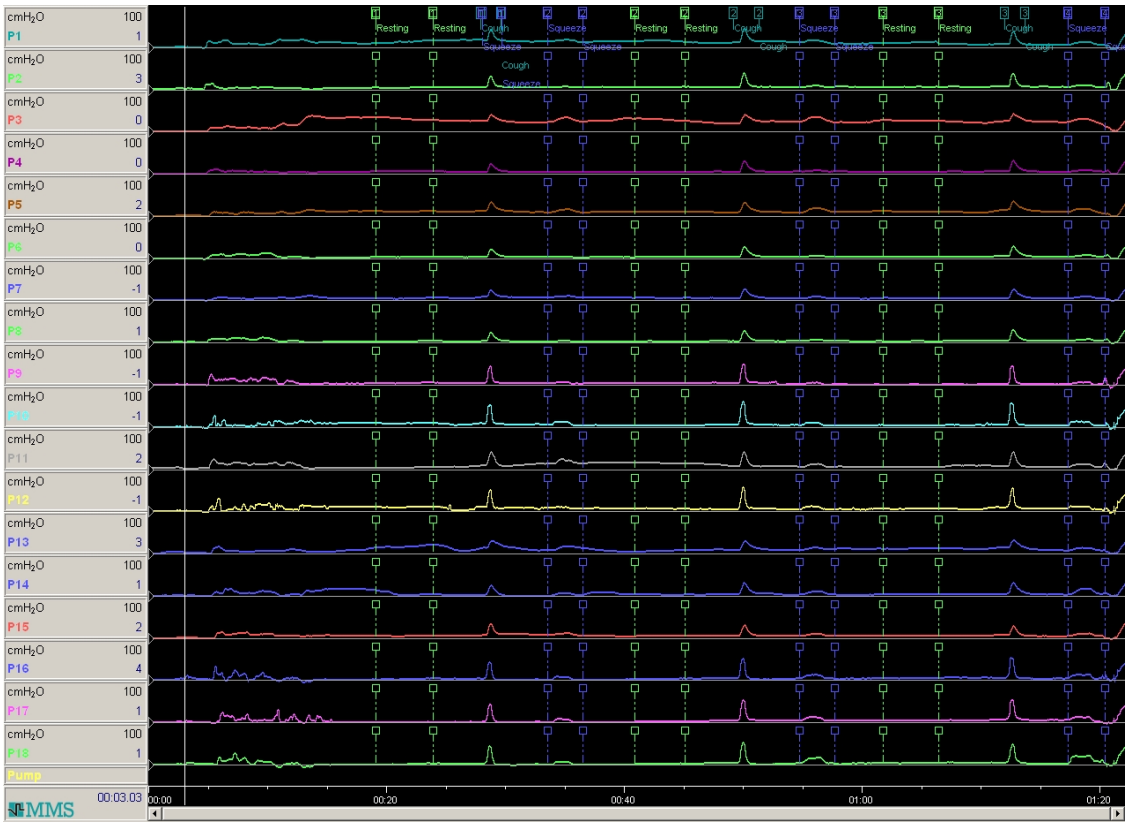
MMS
Resting
Cough
Squeeze
00:00
00:20
00:40
01:00
01:20
01:40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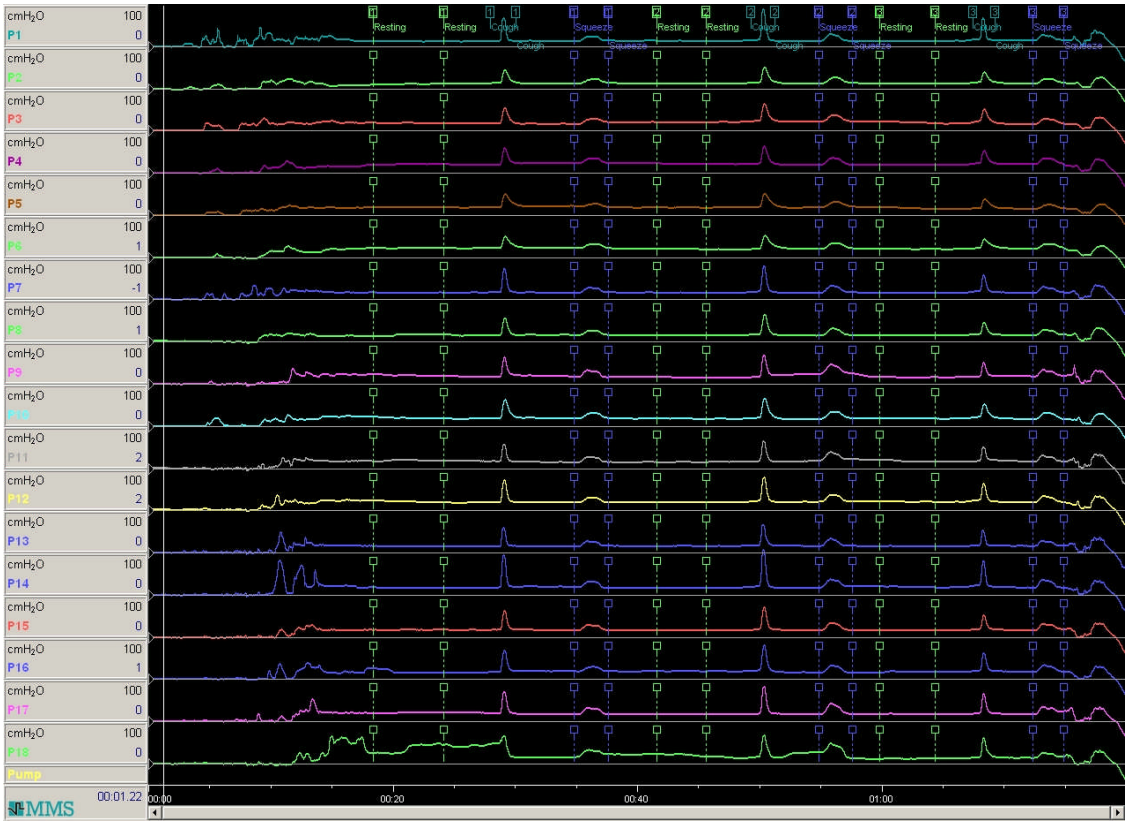
P2 3
P3 0
P4 0
P5 2
P6 0
P7 -1
P8 1
P9 -1
P10 -1
P11 2
P12 -1
P13 3
P14 1
P15 2
P16 4
P17 1
P18 1
Pump
00:03.03
MMS
Resting
Cough
Squeeze
00:00
00:20
00:40
01:00
01:20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P4
P5
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P7
P8
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P14
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Cough
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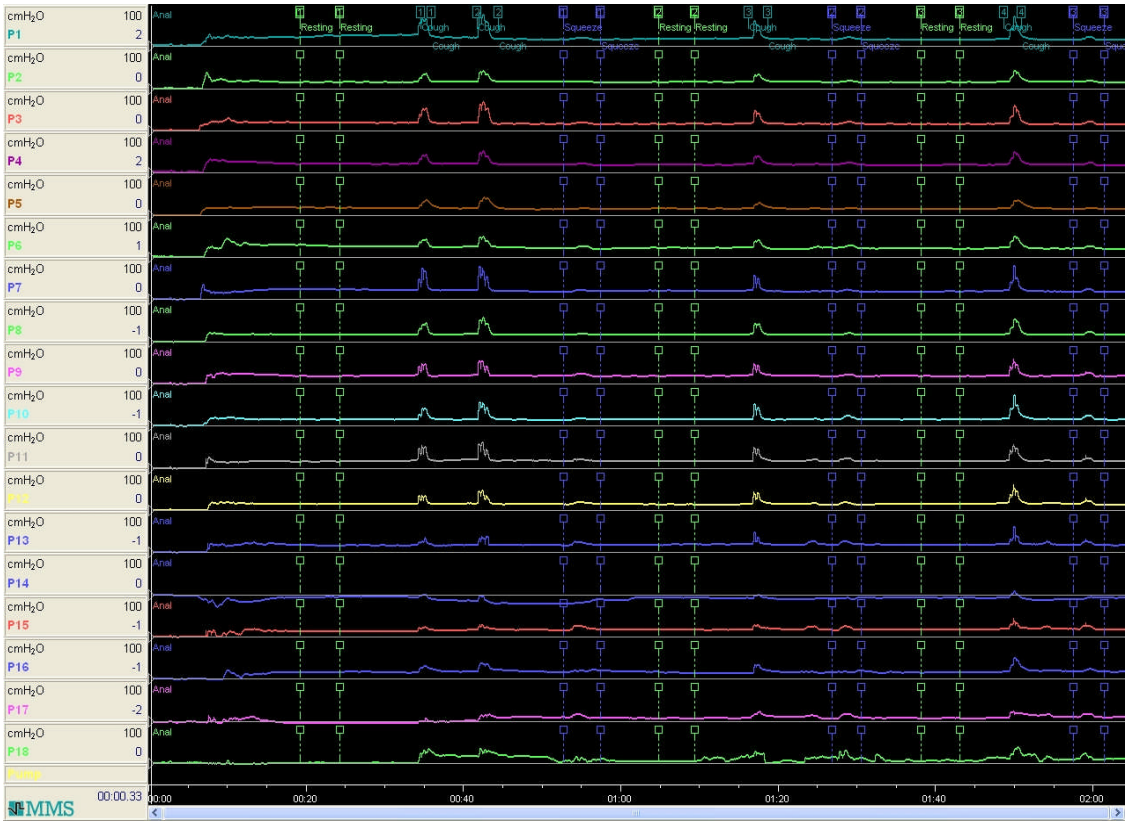
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P7
P8
P9
P10
P11
P12
P13
P14
P15
P16
P17
P18
Anal
Resting
Cough
Squeeze
00:00.33
00:00
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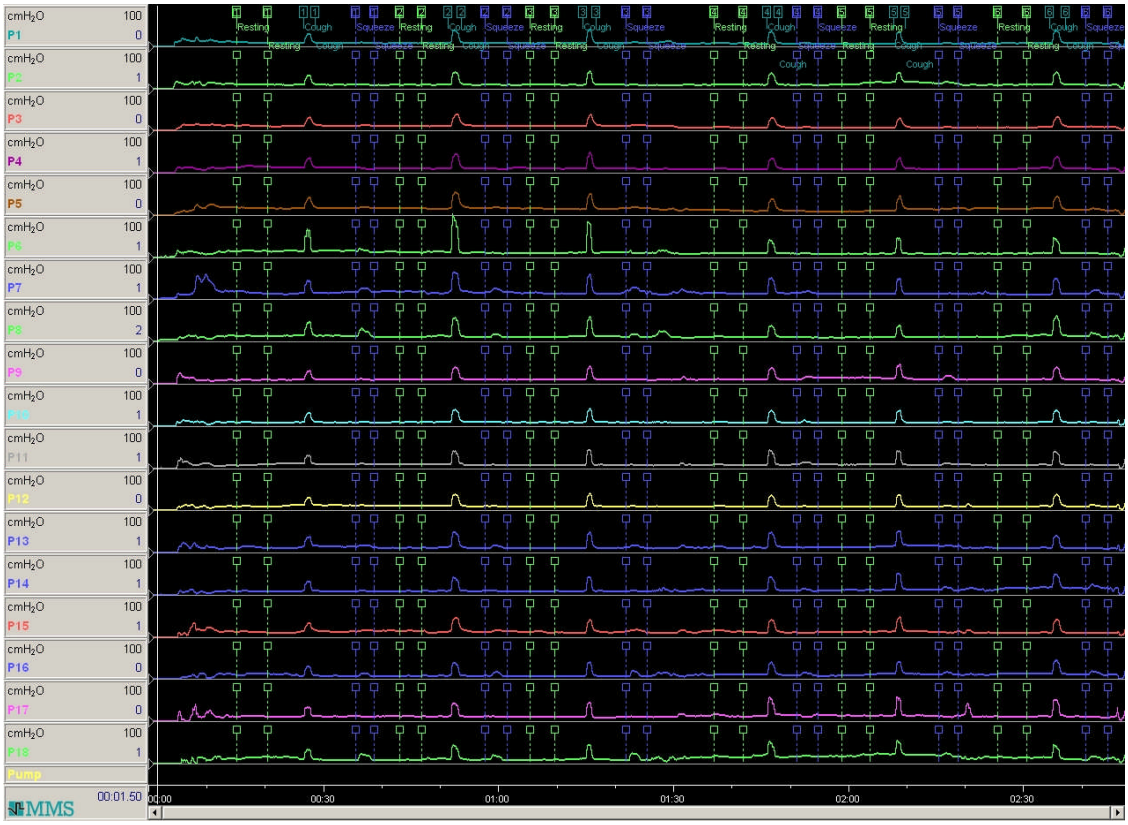
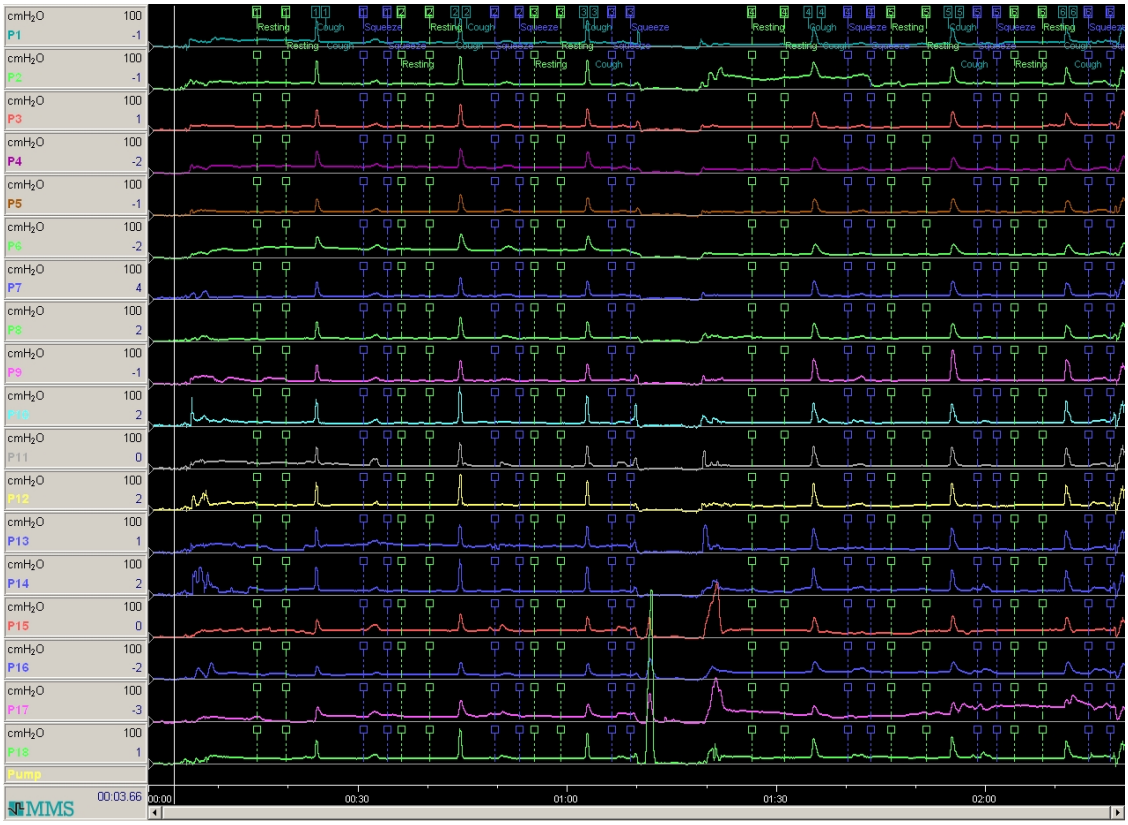
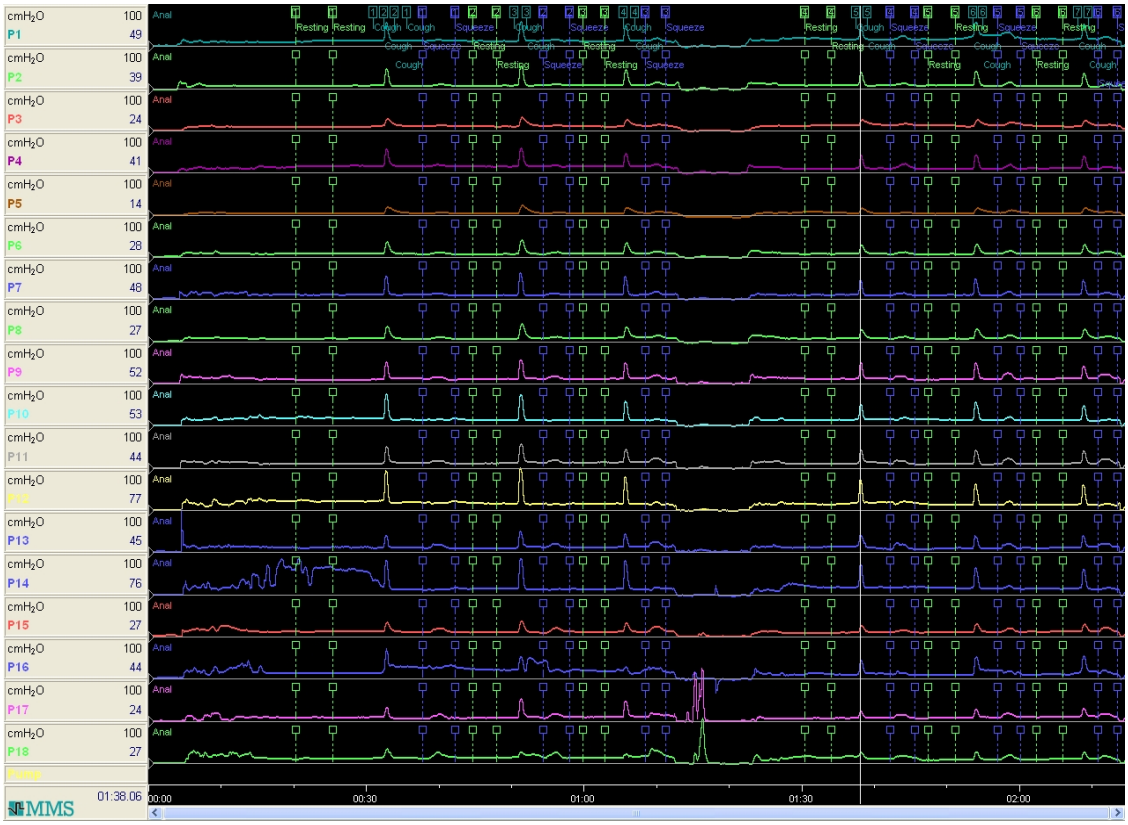
01:00
01:20
01:40
02:00

8.4.2 Vaginal manometry traces from symptomatic patients during rest, squeeze and cough with 90 degree rotation of catheter.



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P17 24
P18 27
Anal
Resting
Cough
Squeeze
MMS
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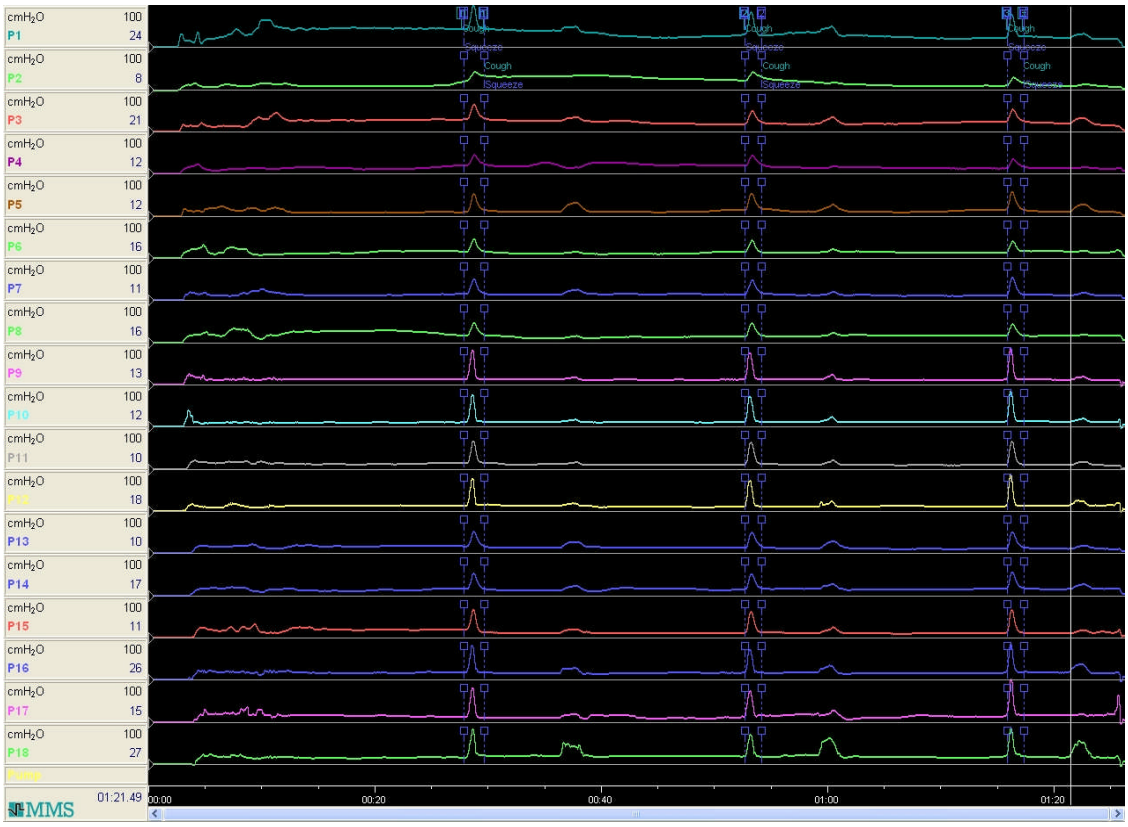
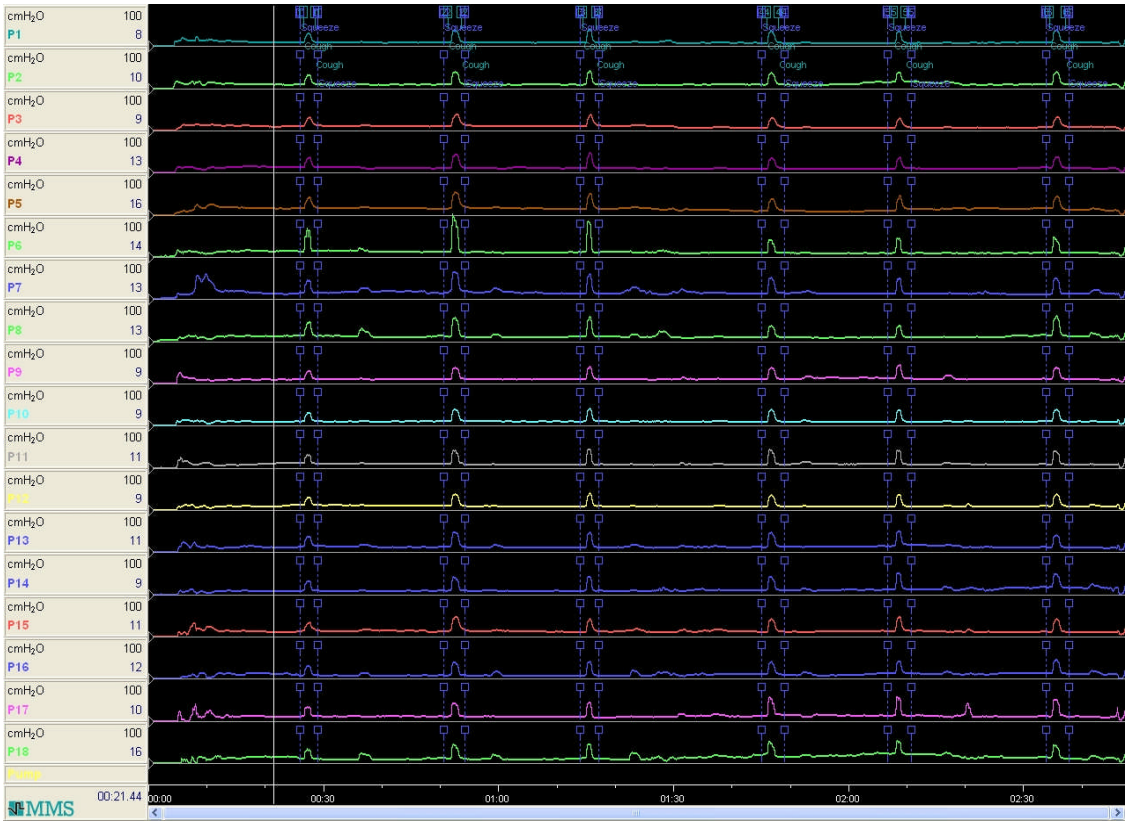
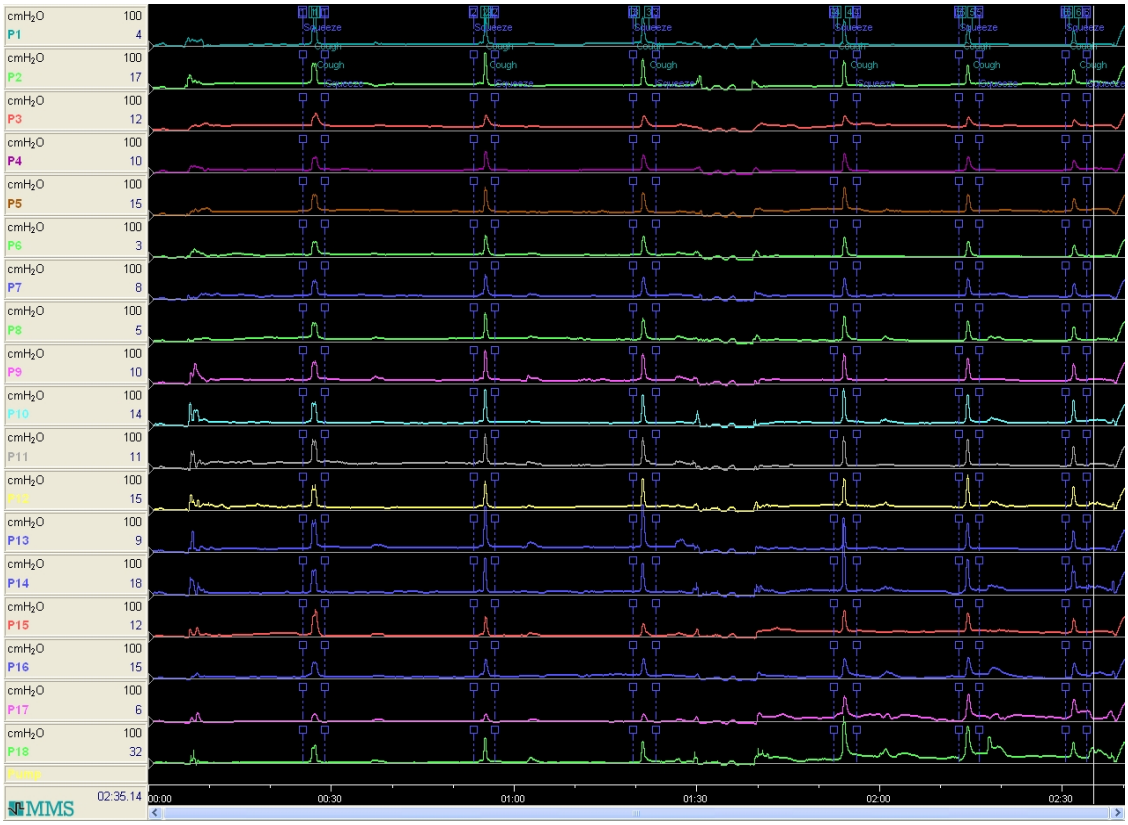
8.4.3 Vaginal canal pressures recorded during cough in symptomatic patients.



8.4.3 Vaginal canal pressures recorded during cough with 90 degree catheter rotation in symptomatic patients.

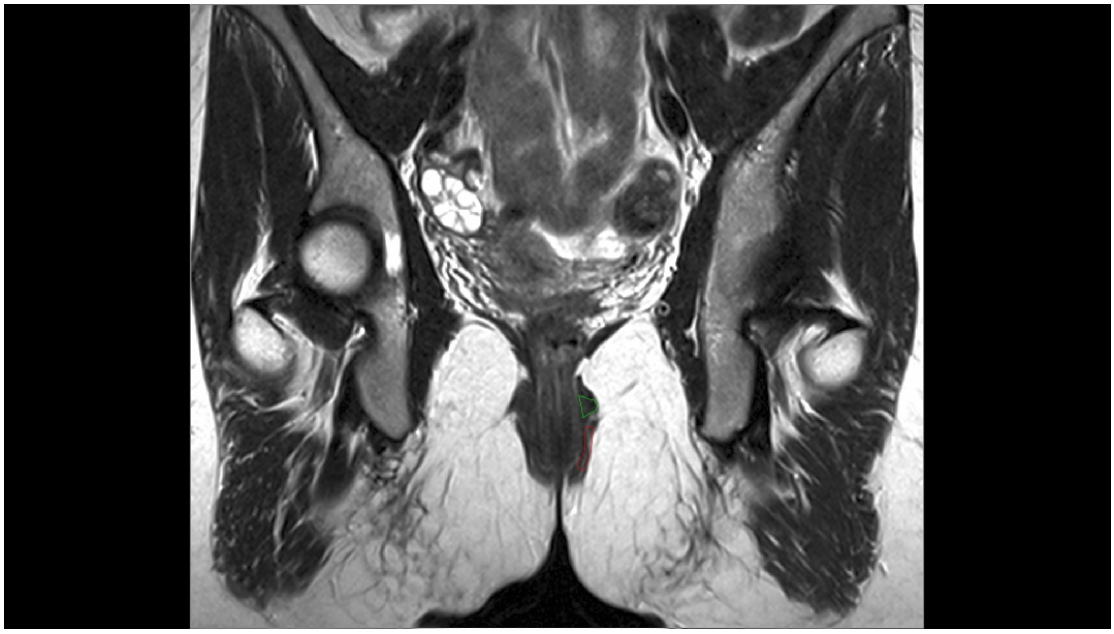


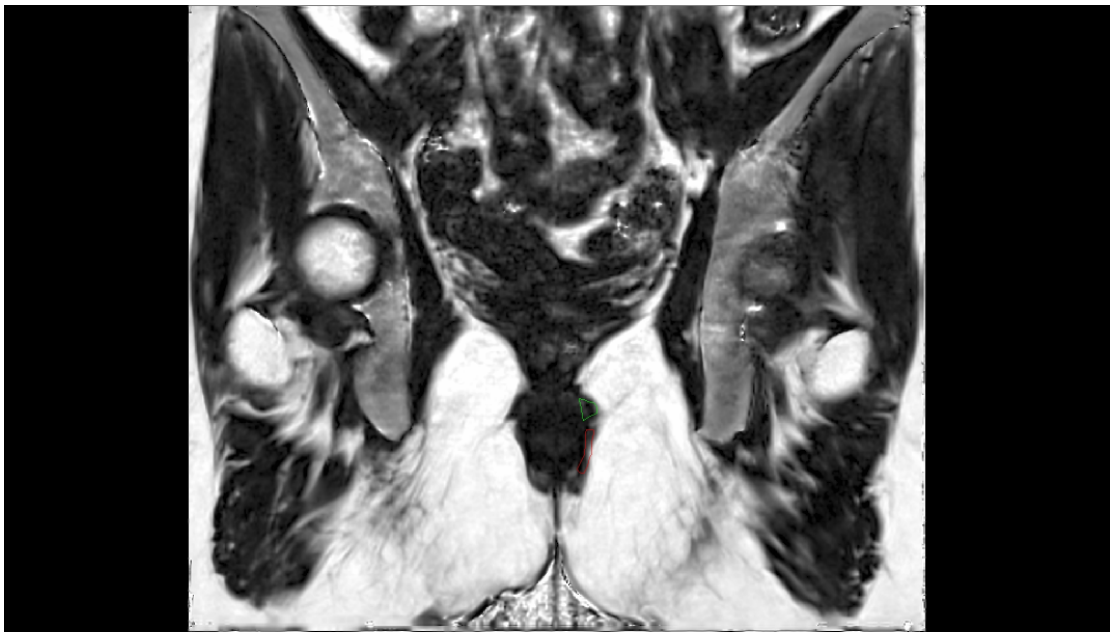


8.5 Appendix 5

Example MRI images with transfer of regions of interest from T2 weighted MR images to corresponding fat fraction maps

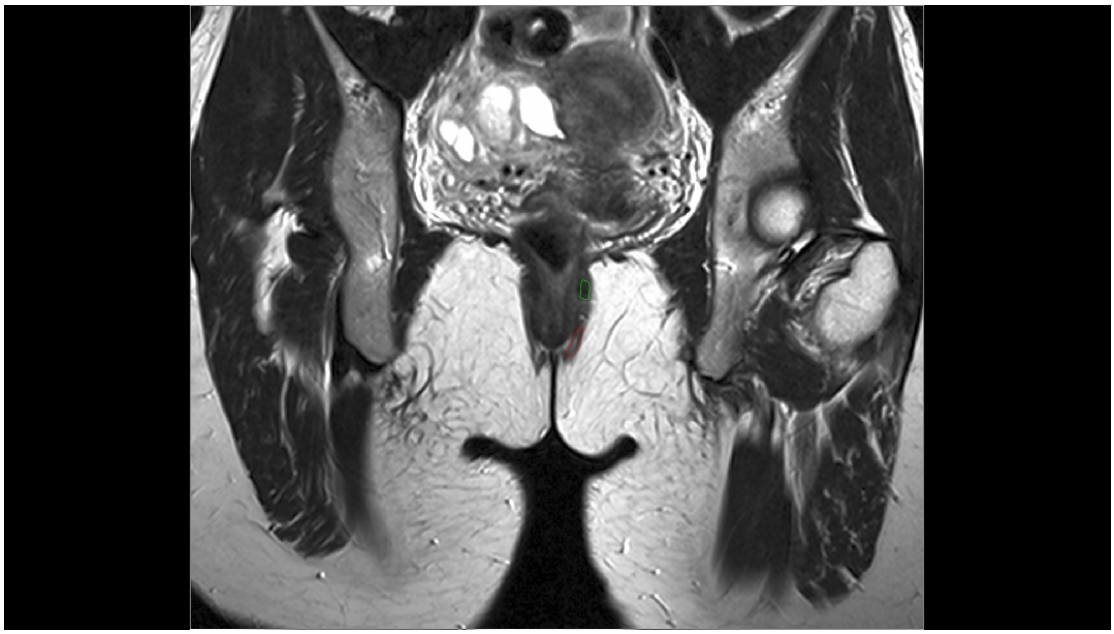
8.5.1 Grade 1 atrophy

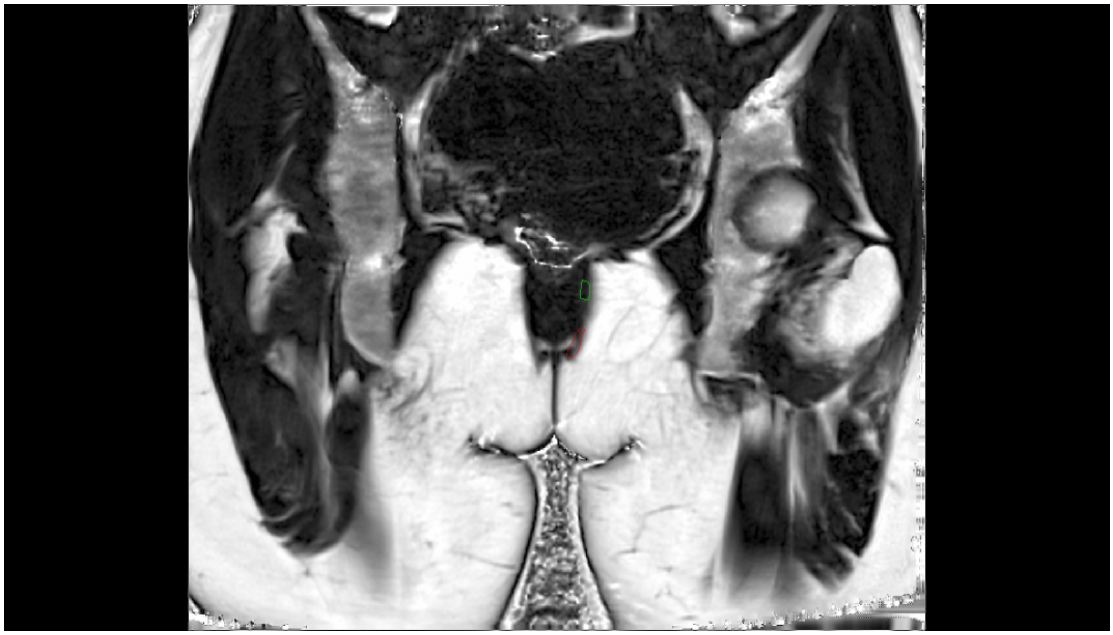




8.5.2 Grade 2 atrophy

Subject 1





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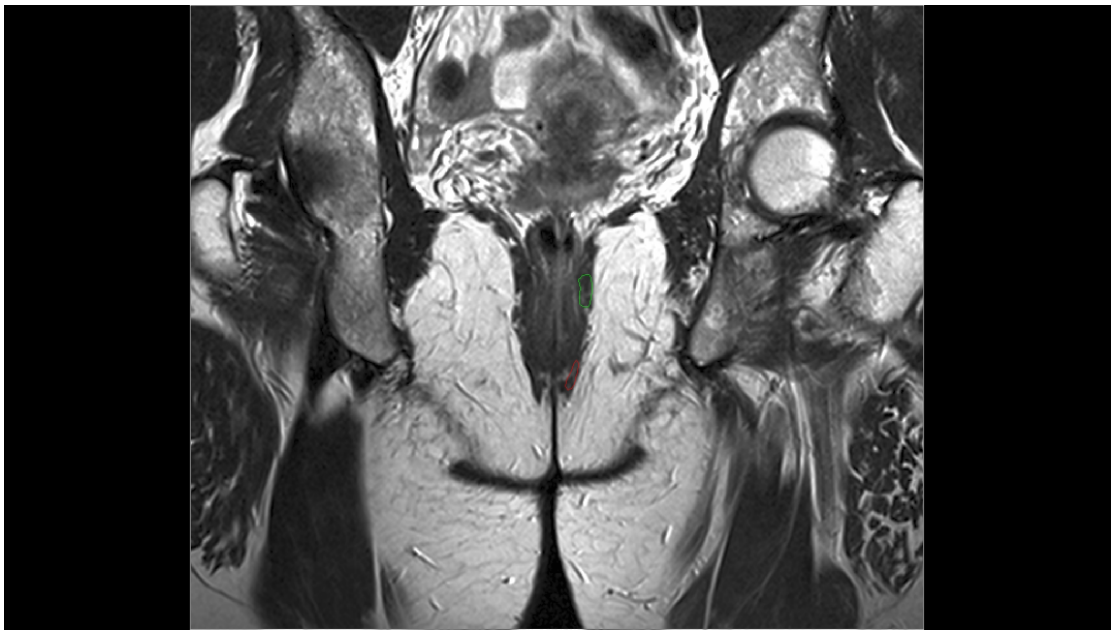

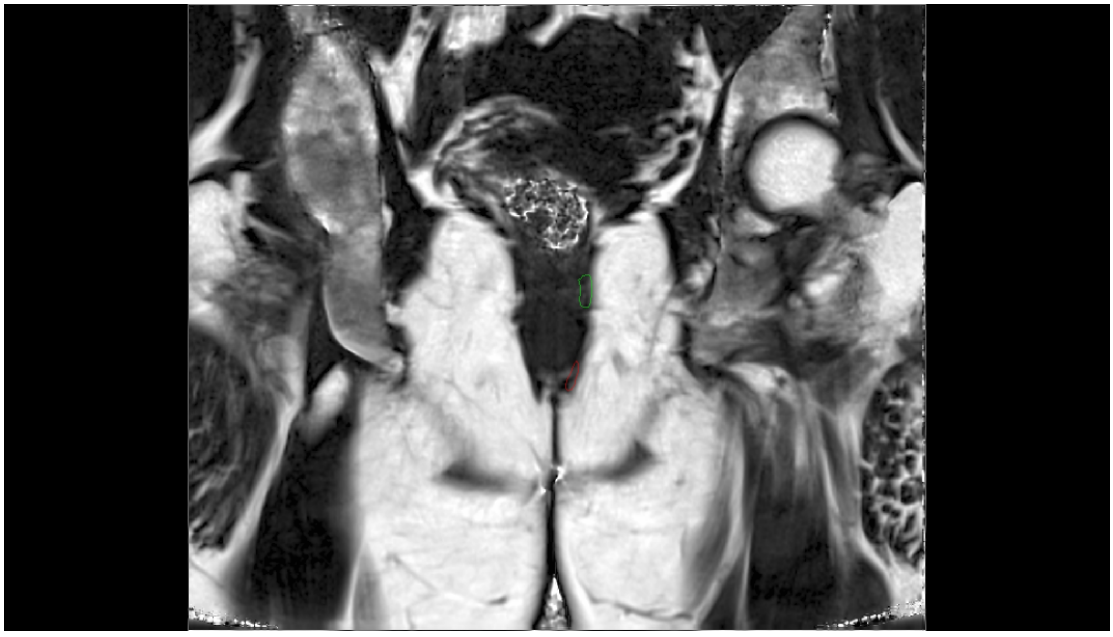

8.5.3 Grade 3 atrophy